A Physician's Guide to Pain and Symptom Management in Cancer Patients

3rd edition

Janet L. Abrahm, MD

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THIRD EDITION

Janet L. Abrahm, MD

With Amanda Moment, MSW, LICSW
and Arden O'Donnell, MPH, MSW, LICSW

Johns Hopkins University Press
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To my parents, Helen and Paul Abrahm;
my brothers, Stanley and Donald Abrahm;
and my aunt, Ruth Garner

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Acknowledgments

First Edition

There are many people to whom I am indebted and for whose help I am very grateful. This book was inspired by my patients and their families, who have taught me much and whose wisdom, I felt, should be shared. I owed it to them and to their memories to help other clinicians reduce the suffering of patients with cancer and minimize the pain of their survivors.

I have also learned a great deal from the medical, nursing, pharmacy, and clinical psychology students with whom I have worked, and the medical interns, residents, fellows, nursing personnel, social workers, pastoral counselors, and ward clerks who have helped me care for my patients. Some of the most important insights I have gained over the years came from interactions with them.

I am grateful to a number of colleagues and teachers whose example sustained me as I worked to relieve the distress of cancer patients and the bereaved families they left behind. First among these are Elizabeth Quinlan-Bohn, certified physician assistant, and Mary Cooley, PhD, OCN, CRNP. Elizabeth embodies the spirit of hospice and commitment to patient care. Her gentle good nature, extraordinary compassion and professionalism, and attention to the physical and spiritual comfort of her patients set a standard that all who work with her seek to emulate. Mary shared with me her office and her insights into grief, bereavement, and the needs of cancer patients and their families; and for a number of years she has supported me in my clinical and educational efforts in palliative care. I must also include the former members of the Philadelphia Veterans Administration Hospice Consultation Team: Jule Callahan, RN, MPH; Debi Selm, MSN, OCN, CRNP; Kathy Rossetti, MSW; Lucy Pierre, MDiv, CPE; Lisa Davis, PharmD; Motria M. Krawczeniuk, PharmD; and Denise Daily, RD.

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Malcolm Cox, Kathleen Foley, Robert Kaiser, Michael Levy, Ruth McCorkle, Russell Portenoy, Marcelle Shapiro, David Weissman, and Charles Von Gunten.

For editorial advice and unwavering support for this project, I thank my husband, David R. Slavitt, and my editor, Jacqueline Wehmueller.

Second Edition

One year after the first publication of this book, in January 2001, I joined the Division of Psychosocial Oncology and Palliative Care at the Dana-Farber Cancer Institute and moved into new digs in Cambridge, Massachusetts. For both my new job and my move to Cambridge, and for many of the new insights you will find in this revised and updated edition, I want to thank Dr. Susan Block. Susan is our division chief, and her vision and leadership make the work we do possible. I would also like to acknowledge the support and guidance of the members of our Pain and Palliative Care Team: Maureen Lynch, MS, APRN, BCPCM, AOCN; Mary Jane Ott, MN, MA, RNCS; Bridget Fowler, PharmD; Sarah Murphy, LICSW; David Giansiracusa, MD; our fellows past and present: Vicki Jackson, MD, MPH; Lauren Dias, MD; Alexie Cintron, MD, MPH; Mary Buss, MD; and Jacob Roth, MD; our program assistants and managers, past and present: Cheryl Adamick, Shawn Curtis, Kristen Morda, Nina Gadmer, and Don Cornuet; and our collaborators in Chaplaincy, Katherine Mitchell; in Ethics, Dr. Martha Jurchak; and in the Anesthesia Pain Service, whose chief is Dr. Edgar Ross.

I have had a great deal of assistance from other colleagues at Dana-Farber and at the Brigham and Women's Hospital. I am very lucky that Dr. Mary Cooley, whose help I acknowledged in the first edition, has relocated to Dana-Farber, and we continue our close collaboration. For their reviews of portions of the new edition, I would like to thank Dr. Edgar Ross; Dr. Laurie Rosenblatt; Ilene Fleischer, RN; and Diane Bryant, RN. For their support of our Pain and Palliative Care Program, I would like to thank the leadership at Dana-Farber, including Dr. Edward Benz, Dr. Lawrence Shulman, Dr. Jim Griffin, Dr. Lee Nadler, Dr. Robert Mayer, Dr. Philip Kantoff, James Conway, and Dr. Patricia Reid Ponte.

I would not have embarked on this second edition if it were not for the readers of the first, who found it useful and to whom I promised corrections of several errors they discovered! Finally, I need to acknowledge the physicians, nurse practitioners, nurses, and social workers at Dana-Farber who have so generously welcomed our team as collaborators in the care of patients and their families. The work with them is what sustains me, and it is what I have learned from them that I hope to share with the readers of this book.

For their encouragement, patience, and valuable editorial assistance, I again thank my husband, David R. Slavitt, and my editor, Jacqueline Wehmueller.

Third Edition

It is now December 2013, and I have been working at Dana-Farber Cancer Institute (DFCI) and Brigham and Women's Hospital (BWH) for thirteen years. Since the second edition of this book was published, we have come a long way. Palliative care is now an integral part of the fabric of both institutions. I am now a member of a Department of Psychosocial Oncology and Palliative Care and, until July 2013, was chief of its Adult Palliative Care Division. Palliative care has also come a long way throughout the United States. Hospice and Palliative Medicine became an officially recognized subspecialty in 2006 and gave its first certifying examination in 2008. I was privileged to be among the group who wrote that exam, and I am grateful to my colleagues on the examination writing committee for all they taught me in the six years we worked together. I am especially grateful to the chair of that committee, Dr. Charles von Gunten, my friend and mentor in palliative care, for all the wisdom he has shared with me over the years. Surgeons, radiologists, pediatricians, internists, family physicians, neurologists, psychiatrists, physiatrists, emergency medicine specialists, anesthesiologists, and gynecologic oncologists have all become board-certified in Hospice and Palliative Medicine and entered the field.

With the recognition of our work as deserving subspecialty recognition, I hope that an understanding of generalist level palliative care will soon become a required competency for medical students, residents, oncology fellows (and other fellows who often care for patients with life-threatening illnesses), and graduate physicians. It has already become a legitimate field of scholarship. I am grateful to Harvard Medical School for recognizing that in addition to research and medical education, clinical expertise and innovation are legitimate tracks for promotion, and for promoting me to professor of medicine based on my work in palliative care.

I want to acknowledge again the foresight of the leadership of DFCI and BWH, as well as the Partners organization to which we belong, for their continued support of palliative care throughout their institutions. The Department of Medical Oncology within DFCI has been particularly welcoming, and we are integrated into DFCI's outpatient and inpatient activities as well as the training program of the fellows and graduate medical education activities. For this I again thank Dr. Edward Benz and Dr. Robert Mayer and add thanks to Dr. Anne LaCasce, now the leader of the oncology fellowship program.

The courage, humanity, compassion, dedication to their patients, and eagerness to learn more about palliative care of my oncology colleagues at DFCI, and the thousands of practicing oncologists I have met through my educational activities in the years since the second edition appeared, continue to inspire me. To answer many of the questions they asked, I updated this edition and added new chapters on sexuality and family dynamics. Equally inspiring are the nurse practitioners (NP), nurses, physician assistants, social workers, clinical pharmacists, and chaplains who care for these patients and for us on the palliative care teams. My hope is that they will find this book useful in the very difficult work they do.

I am grateful to all the members of the Adult Palliative Care Division at DFCI and want especially to acknowledge the unique talents of Amanda Moment, MSW, LICSW, and Arden O'Donnell, MPH, MSW, LICSW, who contributed such informative and useful chapters to this edition. I owe special thanks for the support, friendship, and wisdom of Drs. Kathy Selvaggi and Jane deLima Thomas, and to Katie Fitzgerald Jones (our lead NP), Bridget Fowler Scullion (our lead clinical pharmacist), Phil Higgins (our lead social worker), Katherine Mitchell (our now-retired chaplain), and Ian Nagus (our lead physician's assistant). Suzanne McHale supported me (and the whole division) for many years before moving on to her new position at DFCI, and Cheryl Adamick, Ashley Lewis, and Jennifer Dowd are now my go-to people. Nothing would happen without them!

Mary Cooley, PhD, OCN, CRNP, is now a nationally recognized, award-winning nurse scientist. I am grateful that Mary continues as my great friend and research mentor and leader of the innovative projects that we hope will bring the materials contained in this book into the day-to-day care of cancer patients. We have translated our evidence-based treatment suggestions into computable algorithms. At DFCI, we piloted the system using these algorithms, creating a report for oncologists that details personalized treatment recommendations for pain, dyspnea, anxiety, depression, and fatigue for each of their patients at every visit. Mary continues to inspire me and challenge me to be more creative and inventive, while remaining practical.

For truly broadening my horizons and insisting that I try my best to live at "10,000 feet" instead of in the trenches, I want to acknowledge my brothers, Stanley and Donald Abrahm, and my friend and mentor Dr. Eric J. Cassell. Through our many conversations, arguments, and working sessions, Eric has helped me move my focus and enhance both my connections to patients and my effectiveness as a teacher. I also thank Adrianne Vincent, who introduced me to the practice of mindfulness meditation, and who has studied with me as part of

her work at the Harvard Divinity School. Adrianne generously shares her wisdom and training with my staff and our fellows. She also reviewed and updated Chapter 7.

For their encouragement, patience, and valuable editorial assistance, I again thank my husband, David R. Slavitt, and my editor, Jacqueline Wehmueller.

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Introduction

Despite extensive efforts to prevent cancer and find its cure, each year cancer causes hundreds of thousands of men and women to suffer. Many are cured, but along the way they may have undergone devastating suffering arising from physical, psychological, spiritual, and financial problems. Less fortunate patients, whose cancer is resistant to curative or even life-prolonging therapies, may be told, "*I'm sorry. There is nothing more we can do for you.*" But this is not true. Suffering can be prevented or treated whenever it occurs, whether at diagnosis or during curative therapy, or if the cancer recurs. Patients can heal even as their disease progresses.

In addition to disease-oriented treatments, cancer patients need attention to themselves as whole persons as well as comprehensive treatment for the physical, psychological, social, and spiritual disorders brought on by the disease or by the therapies directed against it. They will benefit from clinicians (physicians, nurses, nurse practitioners, physician assistants, clinical pharmacists, chaplains, social workers, psychologists, and psychiatrists) who are expert at relieving their pain or other troubling symptoms; who can understand the causes of their suffering and what it would take to make them whole; who will make the person, not the disease, the focus of their attention; and who can anticipate patients' hidden concerns, answer their unasked questions, and help them deal with their fears.

There are a number of oncology texts that focus on the details of disease-oriented treatment. *A Physician's Guide to Pain and Symptom Management in Cancer Patients* complements such texts, concentrating on suffering in patients with cancer and offering symptom-oriented, person-focused treatment. Designed for a busy practicing clinician, it is more thorough than a handbook but less comprehensive than a textbook.

This book will be particularly useful to clinicians who wish to enhance their relationships with patients and their families and expand the focus of their care. Physicians, nurse practitioners, nurses, social workers, and physician assistants who work in primary care, general internal medicine, family practice, geriatrics, or oncology (medical, radiation, or surgical), or with hospice or palliative

care programs, will find information that spans the cancer trajectory from diagnosis to death. I offer help with communication challenges that occur at each stage, address the issues of most concern to patients and their loved ones, describe how to assess and manage the most troubling symptoms, and review how clinicians can provide expert, compassionate care for the dying and their bereaved families.

In writing this book, my social work colleagues and I relied on the work of experts in the field whose remarkable research and untiring efforts have delineated regimens and approaches that have revolutionized symptom management and palliative care. Their work is referenced in the bibliography at the end of each chapter and in the bibliography for clinicians at the end of the book. I drew also from the lessons I learned from my patients and their families during my thirty years as a teacher and clinician, as a relative and friend of people who have had cancer, as well as from my students and my colleagues. The clinical stories that appear in the book were crafted from these experiences.

Superior communication skills and technical expertise are both required if we are to succeed in relieving the distress of cancer patients, and the organization of this book reflects these dual requirements. In Part I, Hidden Concerns, Unasked Questions, I discuss the unique issues we need to address if we are to provide optimal care to cancer patients and their families along with suggestions for how to address these issues. Arden O'Donnell's chapter helps us understand how families work and how best to work with them. Part II, Pain Control, Symptom Management, and Palliative Care, complements Part I. It contains Amanda Moment's discussion of sexuality and intimacy in cancer patients, along with my detailed presentation of the technical aspects of symptom assessment and management; it also includes therapeutic protocols for the most common problems faced by patients with cancer, including those that occur in the patient's final days. In both Part I and Part II, clinical scenarios illustrate many of the dilemmas presented by patients and their families. Important practice points are highlighted throughout the text and in numerous tables.

Part I. Hidden Concerns, Unasked Questions

"What is wrong with me? Am I dying?"

The questions begin even before the official cancer diagnosis is made, and they continue throughout the course of treatment, whether the patient is cured or enters the cycle of relapse and retreatment that ultimately leads to death. In this way, of course, cancer patients are not unlike any other patients, who de-

liver the most surprising replies to, *"What brought you here today?"* My father, a general internist who was in private practice for more than fifty years, cautioned me that it is usually more important to listen carefully for what patients don't say than to what they do.

This is certainly true for patients with cancer, whose concerns often differ in significant ways from those of patients without cancer. The proximity of death and the specter of helplessness, grief, suffering, and loss of dignity demand their attention. Most often, however, patients and their families do not openly share with their physicians their fears about the disease, the problems it produces, or the agents used to treat them.

Mrs. Ventimilio,* for example, who had been cured of a small, localized breast cancer for over ten years, unexpectedly appeared at my oncology office one day for a "full check-up." During the course of the evaluation, she admitted that she had gone to a funeral the previous day and had begun to wonder whether she was really cured or whether the breast cancer was lying undetected inside her. Had I failed to discover that fear, I would not have been able to eliminate it or the stress it was causing.

Another patient, Mr. Ashton, who I had been treating for metastatic lung cancer, asked me for pills so he could commit suicide "when the time is right." As we discussed his request further, it appeared that he was concerned not for himself but for his elderly wife: he feared that she might ruin her health trying to care for him as he died. As he came to understand about hospice programs and how hospice personnel and his friends and family could work together, he, too, was reassured. In both these cases, the hidden concerns, the unasked questions, were the real source of distress.

Part I addresses the unique concerns of cancer patients and their families and offers ways of dealing with the unasked questions. Over the years, either as an oncologist or as a palliative care physician, I discussed many difficult issues with patients and their families, and some of these talks went much better than others. I include a number of sample dialogues that demonstrate what I have learned about how to communicate concern, elicit useful responses from patients and their families, and satisfy their needs.

Chapter 1. Early Days

This chapter may be especially helpful for clinicians who are just starting to take responsibility for telling patients bad news, initiating advance care planning,

*All names of patients and their physicians are pseudonyms.

and discussing a prognosis that may be limited to a few more months of life. It begins with a review of what makes a conversation difficult; offers techniques to analyze what about our own experiences, feelings, and identities contributes to our unease as we prepare for the meeting; and explains how mastering the "third conversation" can enhance the outcomes. By understanding what we are bringing to the conversation, we can better address the concerns of patients and their families. A particularly difficult discussion, especially for a beginner, is telling a patient that he or she has cancer or that the cancer has recurred. Early Days includes a review of techniques for breaking bad news and for dealing with the patient's response.

Of interest to more experienced clinicians may be the discussion of why physicians can be reluctant to raise the subjects of advance directives and resuscitation or of prognosis as well as the methods I offer for presenting these issues to patients and their families. I also review the new advance care planning documents, Physician/Medical Orders for Life-Sustaining Treatment (POLST/MOLST) forms, cultural considerations in advance care planning, the role of the pre-meeting before the family meeting, and the varieties of shared decision-making that clinicians can use in these discussions. Finally, I discuss how to manage conflict, and how ethics consultation teams can partner with the clinical team when a value conflict prevents the teams and the families from reaching consensus.

Chapter 2. Helping Patients Accept Opioid Pain Medication

A major source of hidden concerns and unasked questions is the need of some patients to take opioids for relief of pain or dyspnea. Unless a number of barriers are overcome, patients won't take their medication and will continue to suffer. Chapter 2 addresses the misconceptions of patients and their families about the use of opioids: becoming addicted, having no effective medication later if the symptom worsens, becoming constipated or "doped up," or going against the teachings of their religion. This chapter provides examples of patients and families with such concerns, as well as suggestions for anticipating and overcoming them. I also review other impediments to compliance, including patients' reluctance to admit how much pain they are experiencing and the role of hidden agendas in impairing your ability to relieve their pain. Here, we may expect to confront guilt, denial, and anger, all of which I discuss. Finally, I explain how educating colleagues can enhance patients' compliance.

Chapter 3. Working with Patients' Families

In this chapter, Arden O'Donnell, MPH, MSW, LICSW, who is a member of our palliative care consultation team, shares her review of the literature and her hard-earned insights as a clinician to describe the basics of how families function. She first describes family structure, showing us how to identify its elements and why it's important to identify key family members and the role that each family member plays, including our patient's role.

She next gives us tools to assess how the family functions, which will enhance the success of any family meeting, whether it be about a symptom management regimen or advance care plans. Arden describes how to look at each family as a system and gives us scales on which we can locate the level of family cohesion (on a scale that ranges from "disengaged" to "enmeshed"), and the level of family flexibility ("rigid" to "chaotic"). She also helps us see how much family members communicate which each other, which turns out to be much more variable than I had ever imagined. She ends the assessment section with a discussion of the role of culture.

Finally, Arden describes situations in which oncologists and their teams should get expert help from psychiatrists or expert social workers or nurse practitioners: when there is longstanding conflict in the family; when the patient or a family member has a personality disorder or severe mental illness or is addicted; or when there is a history of domestic violence.

Chapter 4. Approaching the End

As death approaches, other communication problems surface. Chapter 4 deals with the most common of these. Many difficulties arise from misunderstandings among the clinician, the patient, and the family about the true extent of the disease, the goals of treatment, and the expected outcomes of whatever therapy is chosen. Other issues, as this chapter explains, are the consequence of differences in the priorities that patients, families, and physicians place on the various symptoms the patient is experiencing and the remedies that are reasonable to relieve them.

Another challenge is helping patients and their families make the transition to comfort care. I explain how the rigors of the chemotherapy schedule have caused most patients and their family caregivers to stop being involved in work, their community, and even their family. If patients and their families reintegrate important activities into their lives, their days can be full without chemotherapy, and it will be easier to accept that the patient will no longer benefit

from it. I also suggest how to readdress the issues of resuscitation and I review the concerns of two groups of patients who, despite very advanced cancer, often still want to be resuscitated: dying parents who have young children, and families and patients who are waiting for a miracle. Once the patient and family have accepted comfort care, hospice programs can help clinicians and their office staff members alleviate family insecurities. I detail hospice eligibility criteria for patients who do not have cancer and the levels of clinical care that hospice programs provide (a detailed description of hospice services is given in Chapters 9 and 10).

House staff who help us care for dying patients frequently ask us, *"How do we know when it's time to stop what we normally do?"* I answer their question in this chapter and review our experience with the grief rounds we hold for house staff. Despite these efforts at providing the best of care, some patients with advanced disease ask us to assist them in committing suicide. I review the hidden concerns underlying these requests and offer sample dialogues and information that will be useful in addressing them. Finally, I discuss self-care, including compassion fatigue, a common consequence of coping with the reality of caring for so many patients who suffer and die. Compassion fatigue is an occupational hazard for oncologists and the clinicians they work with, and this chapter contains practical information for how to recognize it in a colleague or in yourself, and how to prevent or reverse it.

Part II. Pain Control, Symptom Management, and Palliative Care

Part II continues the comprehensive approach to patient suffering that is the core of a palliative care approach, including a symptom assessment and management handbook. Its six chapters review how to assess pain and treat it by pharmacologic and nonpharmacologic means; how to work with patient concerns about sexuality and intimacy; how to detect, assess, and address distressing problems other than pain; and how to care for patients in their final days and for their bereaved families.

Chapter 5. Assessing the Patient in Pain

A thorough pain assessment reveals the cause or causes of the pain and the factors that exacerbate the experience of pain for each patient. It is the foundation on which both pharmacologic and nonpharmacologic therapies rest. Chapter 5

reviews the components of a comprehensive pain assessment, provides examples of several measurement tools available for this purpose, describes tools to detect excessive alcohol use and to determine a patient's risk for opioid abuse, defines the characteristics of the various types of pain, and describes in detail a number of cancer-related pain syndromes that occur only rarely in patients without cancer. At the end of the chapter, I discuss how to determine whether the patient is suffering from anxiety, depression, delirium, or social or spiritual distress. These can exacerbate the experience of pain and can in themselves adversely affect the quality of life of patients and their families.

Chapter 6. Pharmacologic Management of Cancer Pain

This chapter reviews pharmacologic therapy, the cornerstone of cancer pain treatment. I discuss the use of nonsteroidal anti-inflammatory drugs and opioids, delivered by the oral, transmucosal, topical, transdermal, rectal, intravenous, subcutaneous, or spinal routes, and how to choose among these agents and routes. I include a specific discussion of the use of methadone for cancer pain. I also discuss treatment of the common opioid-induced side effects: constipation, nausea, sedation, opioid overdose, opioid neurotoxicity, delirium, and respiratory depression. Adjuvant pain relievers are then reviewed, including adjuvants for nerve pain (such as corticosteroids, anticonvulsants, tricyclic antidepressants, baclofen, clonidine, and ketamine), agents for bone pain (such as NSAIDs, corticosteroids, external beam radiation and radiopharmaceuticals, bisphosphonates, receptor activator of nuclear factor κβ ligand [RANK-L], vertebroplasty and kyphoplasty, and radiofrequency ablation), neuroleptics, and skeletal muscle relaxants. Also included are anesthetic methods, such as topical and oral agents, neural blockade, and neuroablation. Special mention is made of the considerations needed in treating older patients, including those who are cognitively impaired, and patients with active or past histories of substance abuse, including patients who are taking methadone or buprenorphine.

Several tables detail the NSAIDs and opioid drugs available, their formulations, the doses recommended, a cost comparison, and caveats about their use; other tables list similar information for laxatives, antiemetics, psychostimulants, agents that treat delirium, adjuvant agents for neuropathic pain, antidepressants, adjuvants for bone pain, and topical and oral anesthetics.

Practical suggestions for common clinical situations are offered: how to start patients on opioids; how to change the opioid dose, route, or agent safely; and how to relieve excruciating pain rapidly.

Chapter 7. Nonpharmacologic Strategies for Pain and Symptom Management

The National Center for Complementary and Alternative Medicine has defined five domains of complementary and alternative therapies: (1) alternative medical systems, (2) manipulative and body-based methods, (3) mind-body interventions, (4) biologically based therapies, and (5) energy therapies. In this book, I do *not* review the biologically based therapies, which include special diets, such as the Atkins or Ornish diets, herbal treatments, megadose vitamin therapy, or use of particular substances not proven effective by conventional medical studies, such as laetrile. I also do not review energy therapies such as qi gong, Therapeutic Touch, Reiki, and healing touch, but I do provide references for those who are interested in these areas.

I discuss what I consider to be those nonpharmacologic techniques for which there is the most evidence supporting their effectiveness in relieving pain and other sources of distress in cancer patients. These include acupuncture/acupressure and yoga, two of the alternative medical systems involving philosophies and practices that are completely independent of the usual medical approach. I also discuss manipulative and body-based methods, including cutaneous interventions, massage and vibration, transcutaneous electrical nerve stimulation (TENS), and positioning and exercise. Finally, I review the mind-body interventions that include education; cognitive and behavioral interventions such as diversion of attention, relaxation and breathing, guided imagery, mindfulness meditation, mindfulness-based stress reduction (MBSR), and hypnosis; biofeedback, and music and art therapy. As a hypnosis practitioner, I am more familiar with the use of hypnosis and therefore am able to provide a discussion of some misconceptions that have limited its use, along with a sample relaxation exercise that cancer patients may find useful. I also discuss the role of spiritual counseling, and of speech and language therapy.

Chapter 8. Sexuality, Intimacy, and Cancer

I have had the pleasure and great fortune to work for the past several years with the author of this chapter, Amanda Moment, MSW, LICSW. She is the social worker on the Intensive Palliative Care Unit team at Brigham and Women's Hospital, a respected clinician, and a gifted teacher. In this chapter, Amanda discusses a subject that physicians often know little about: our patients' concerns about how cancer and its treatment will affect their sexuality. We have even less training on how we can talk with our patients and their partners about this subject.

Amanda first reviews why this subject is important, including the positive outcomes that can stem from our becoming more comfortable with and more expert in these discussions. She describes how cancer and related treatments affect sexuality, and then explores clinician barriers to the discussion, and how to approach the subject. She reviews the models and tools available to us and makes practical suggestions for having these much-needed conversations. She ends with a review of special considerations, such as culture, same-sex partners and sexual orientation, aging, concerns of partners and of single patients, and palliative care and sexuality.

Chapter 9. Managing Other Distressing Problems

This chapter continues the symptom assessment and management handbook. The discussion includes anxiety and depression, personality disorders, the role of counseling, oral complications (candida, herpes simplex virus, xerostomia), gastrointestinal problems (ascites, diarrhea, dysphagia, and nausea and vomiting, including treatment-induced nausea and vomiting and bowel obstruction), respiratory problems (dyspnea, cough, hemoptysis, and hiccups), skin disorders (hand-foot syndrome, EGFR-inhibitor-associated skin disorders, fungating skin lesions, pressure sores, and pruritus), insomnia, and hot flashes. I also include the common treatable causes of weakness and fatigue: Eaton-Lambert syndrome, anemia, metabolic abnormalities, anorexia, and malnutrition. Patients and their families commonly believe that enteral or parenteral nutrition will restore patients' strength and prolong their lives. I explain why this is not always the case and why enteral and parenteral feeding are not usually indicated for people with advanced cancer. I also offer coping strategies for patients suffering from weakness or fatigue; they often need to modify their activities so that they maximize what they can achieve despite their diminishing capacity.

The chapter ends with a discussion of hospice and palliative care programs: their philosophy, team members, services provided, and what is included in the Medicare Hospice benefit.

The material in the text is supplemented by tables detailing the drugs and their recommended doses for the problems reviewed.

Chapter 10. The Last Days . . . and the Bereaved

Here I review the art and science of helping the dying and the bereaved. I describe the various aspects of a comprehensive program for care of the dying and support for their families, and make special mention of the challenge of caring

for a dying physician. I further explore the role of the hospice team in ensuring that all the important pieces are in place, including bereavement care. Families often want to know when the patient is approaching the end. I provide the clues that will help in recognizing when patients are making the transition and have only weeks remaining. I revisit families' ethical concerns about pain management and review the doctrine of double effect. Although most patients say they want to die at home, over half will die in the hospital. I therefore describe how to care for patients who die as inpatients: how to support the inpatient ward teams, and how to support the patients' families.

The first part of the chapter, The Dying Patient, includes an outline of the symptom complex of dying patients and some treatment recommendations, including a table of pharmacologic therapies for the most common problems: pain, death rattle, terminal restlessness, dyspnea, delirium, dehydration, massive hemoptysis, nausea, vomiting, and myoclonus. I also provide an algorithm for agitation in the last days. For clinicians who have not been present when one of their patients died, I include some thoughts on how to continue to comfort the newly bereaved. I end this section with a discussion of what our institutions could do for clinicians to help us care for our dying patients.

The second half of the chapter deals with the survivors: how we can continue to help the bereaved family and friends. I discuss the manifestations of loss, grief, and mourning, and the differentiation between grief and depression. I discuss both the "intuitive" and the "instrumental" styles of grieving; intuitive grievers look to us as though they are grieving, but instrumental grievers do not, and we may misunderstand their behavior and not offer the support they also need. I also describe a typical bereavement program through which we can support survivors and educate them about what they can expect to feel, and indicate how to identify those who would benefit from formal counseling, cognitive-behavioral techniques, or informal support groups. The chapter also includes the bereavement materials we used before our institution, Dana-Farber, developed an institute-wide bereavement program.

Finally, I review what is called "prolonged grief disorder"—survivors who delay mourning or who never recover from their losses. I discuss the factors that predispose to this syndrome, provide a screening tool that identifies people at greatest risk, offer suggestions for identifying and providing ongoing support and treatment for them, and describe cognitive grief therapy (CGF), a therapy that is particularly effective for these patients.

Bibliographies for Clinicians and Patients

At the end of the book you will find two annotated listings of additional materials. The first contains materials of interest to clinicians, including information on books, handbooks, journals, patient education materials, videos, websites, CDs, and organizations. The second provides listings of books, organizations, support groups, videos, websites, and CDs that you may wish to recommend to your patients and to families who have no special medical training. I have often been asked to provide such resources, and those I include have been particularly useful for my patients and their families and friends.

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CHAPTER 1

Early Days

Difficult Conversations: Understanding and Mastering Them
- The "What Happened?" Conversation
- The "Feelings" Conversation
- The "Identity" Conversation

How to Break Bad News
- Assembling the Team
- Make Yourself, the Patient, and the Family Comfortable
- Find Out What They Know
- Find Out What They Want to Know
- Tell Them in Words They Can Understand, and in Small Chunks

How to Deal with the Response
- The Role of Silence
- Respond to Their Feelings
- Tell Them the Plan
- Ask Them to Summarize What You Told Them; Ask Whether They Have Further Questions

Provide Psychological Support

How to Raise the Subject of Advance Care Planning
- You Need to Use the "D" Word
- The Patient with Spiritual Concerns

Why Advance Care Planning Is So Difficult for Many Physicians
- Physicians Are Forced to Face Their Own Feelings about Mortality
- Physicians Are Loath to Cause Pain
- Physicians Feel Guilty or Are Afraid of Being Blamed
- Physicians Assume They Do Not Need to Ask; They Know Their Patients' Wishes
- Physicians Feel Impotent to Prevent Death and Have Not Grieved Their Many Losses
- Physicians Have Unrecognized Compassion Fatigue

When to Initiate an Advance Care Planning Discussion; What to Say
- More on Advance Care Planning

Discussing Prognosis
Documentation of Advance Care Plans
POLST and MOLST Forms
How to Discuss Advance Care Planning with the Patient's Family: What Works and What Doesn't
Cultural Considerations
The Role of the Pre-Meeting
When You Have Never Met the Family
Shared Decision-Making
"Ask-Tell-Ask"
Conflict
Ethics Consultations
Summary
Bibliography

The foundation of your relationships with patients and their families is profoundly affected both by how you first tell them they have cancer and by how you deal with their response to the news. The nonverbal clues you provide during these crucial interactions reveal a great deal about how willing you are to discuss their fears and how certain they can be of your ongoing emotional support.

Patients and their families need to know you will help them throughout the course of their illness, especially if it eventually causes their death. You must make it clear that you will not abandon them if the medical treatments lose their effectiveness and will use your expertise to help them achieve the best possible quality of life at every stage of their illness.

Part of your responsibility, then, is to communicate clearly your interest in understanding your patients' values, hopes, and goals so that you can choose treatments that best balance burdens and benefits that are meaningful for them. And, should it become necessary, you will then be able to carry out their wishes regarding resuscitation or prolonged support by a ventilator or feeding tube. What do they need to be able to do for life to be worthwhile? Which kinds of disabilities are tolerable, and which not?

In this first chapter, therefore, I review the components of difficult conversations, including how you can most skillfully "break the bad news," and how you can best respond to the reactions of patients and their families. I also consider how to begin discussions of prognosis and resuscitation and other extraordinary support (advance care planning), and what is known about why such discussions are so difficult to undertake; I include several examples of approaches that

work, as well as some examples of conducting family meetings both when you can and when you cannot involve the patients themselves.

Difficult Conversations: Understanding and Mastering Them

To be able to deliver bad news with skill and compassion, you must prepare yourself emotionally for what is likely to be a very difficult conversation. In rehearsing what you are going to say, you need to be aware of your own feelings about the impending meeting and to analyze carefully all the elements that make this a "room you would rather not enter." What makes a conversation difficult? Members of the Harvard Negotiation Project (the people who brought us the very useful book *Getting to Yes*) lay out the key elements in *Difficult Conversations: How to Discuss What Matters Most*, second edition (Stone et al. 2010). The book is designed for businesspeople, but the principles apply equally well to clinicians.

Stone and colleagues suggest that within any difficult conversation lie three conversations: (1) the "What Happened?" conversation, (2) the "Feelings" conversation, and (3) the "Identity" conversation.

DIFFICULT CONVERSATIONS

The "What Happened?" conversation
Given the same set of "facts," does your story differ from theirs?
Can you move from certainty to curiosity?

The "Feelings" conversation
What are you feeling: Sadness? Anger? Guilt? Frustration?

The "Identity" conversation
Is your sense of who you are being challenged?
Have you lost your balance?

The "Third conversation"
Once you have heard their story and had a chance to share your point of view, create from those a "third conversation" that includes shared goals that you both can work on.

(Adapted from Stone et al. 2010)

These conversations can be illustrated by an encounter I had with Yu Hsin and his wife, Jenny, when I was still a practicing oncologist.

Yu Hsin, a 33-year-old man, had non-Hodgkin's lymphoma of the small bowel. He had been married to Jenny for ten years, and they had three children, 8, 6, and 4 years old. Surgical resection of his tumor was not possible. I had tried several chemotherapy regimens, after each of which the tumor had responded. However, the manifestation of each response was severe gastrointestinal bleeding. I went to visit Yu in the hospital on the day he was going to be transferred to a rehabilitation facility. This had been his third hospitalization for bleeding and near perforation of the intestine because of tumor necrosis. I knew that Yu's bowel would surely perforate if we tried chemotherapy again. The surgeons thought surgery would not be helpful. As I prepared to enter the room, I steeled myself to tell Yu and Jenny that we could not risk any more treatment.

We chatted for a while about the planned transfer, which they both looked forward to. Jenny asked when Yu would be coming back for his next treatment, and I replied that, while I wished I had better news, I thought there was nothing more I could do for him, that he would bleed to death or his bowel would perforate if I continued the therapy. Yu took the news stoically, but Jenny asked angrily how I could stop treating him if his lymphoma was responding to the treatment. She accused me of abandoning them and giving up on Yu.

I could barely look at them. I felt numb and distant, as though observing all of us from far away. I reassured Jenny that we would find something to help Yu, hoping that my saying it would make it so. I told Yu that I was glad he was feeling so much better and that we'd talk about next steps when he came to the office. I could not wait to leave.

The "What Happened?" Conversation

I remember very clearly how I felt as I left the room. I had given other patients bad news that had elicited anger from both the patients and their families, but rarely had I felt so distraught. I did not understand then what was different about this conversation.

Later, using the framework from *Difficult Conversations*, I was able to understand "what happened." As Stone and colleagues put it, there are a number of interpretations of the same "facts." So what were the "facts" here? As I saw it, I had given Yu state-of-the-art treatment that was placing him in danger of bleeding to death or dying from a bowel perforation. It was unfortunate, but it was certainly not fair for them to blame me for the location of the lymphoma. Jenny, I surmised, was in denial about Yu's true condition and the danger further therapy would bring.

As the authors caution, however, "You only know your own story." In shutting down in response to their anger, I was not able to ask Jenny to tell me more about her reaction to my news. To this day, I don't know why she thought we could continue his treatments. Maybe she thought the bleeding was a good sign: that the tumor was being flushed out of his system, and the blood transfusions were bringing in clean, safe blood to replace the cancerous tissue. Maybe she did not think Yu's bleeding was any more dangerous than the monthly bleeding she routinely experienced.

I would have been much more helpful to them had I explored why she was so angry and learned more about her interpretation of Yu's response to his treatments. How I wish I at least had not said, *"There is nothing more I can do for him,"* even as a part of my explanation of why I wasn't offering ongoing chemotherapy. Was that why she felt I was abandoning her and giving up on Yu? I'll never know.

Stone and colleagues would suggest that instead of my "certainty," I should have allowed my natural "curiosity" about the reasons for her response to emerge. I should have made more of an effort to hear what she was trying to tell me. So why didn't I do that? Why did I withdraw emotionally?

The "Feelings" Conversation

I think the key is in my feelings about Yu, not in Jenny's anger. And that gets us to the "Feelings" conversation, which refers to the emotions that are welling up within us that we don't allow to come to the surface and be named. I am sure I felt very sad, not only for Yu but for Jenny and their children. I think I was also feeling guilty, inadequate, and helpless, and these emotions were contributing to my emotional disconnection from Yu and Jenny.

If, before our meeting, I had reflected on how I was feeling, I could have shared at least my sadness with them, rather than presenting a false cheerfulness. I am sure my body language was giving me away anyway, and the dissociation between what they could see and what I was saying must have contributed to their distrust.

Later, I could have shared my guilt, inadequacy, and helplessness with colleagues. I eventually did seek consolation from a wonderful third-year fellow after he told us of the success he was having with one of his patients. *"Your patients always seem to do so well,"* I said. *"I must be doing something terribly wrong with mine."* He laughed, put an arm around my shoulder, and said, *"Janet, I only talk about the ones who are doing well. There are plenty who don't."* He took me to the cafeteria for coffee, helped me explore my feelings, and gave me some strategies for coping with the emotions raised by the work we both did.

The "Identity" Conversation

I probably could have dealt with my feelings if that was all that was going on. But what shut me down was that Jenny's accusations echoed the doubts I was feeling about myself as a physician. As Stone and colleagues say, " 'The Identity Conversation' looks inward: it's all about who we are and how we see ourselves. How does what happened affect my self-esteem, my self-image, my sense of who I am in the world? What effect will it have on my future? What self-doubts do I harbor? In short: before, during, and after the difficult conversation, the Identity Conversation is about what I am saying to myself about me."

What happened to me, *Difficult Conversations* suggests, was that I lost my "balance." My sense of competence, trustworthiness, loyalty, professionalism all were under attack. I reeled not from the blows inflicted by Yu's sadness or Jenny's anger, but from doubts of my own competence as an oncologist that her anger and his despair had triggered. Unaware as I was of this disequilibrium, I shut down and used only my "executive functions" for the rest of the conversation, going through the motions, and reinforcing Yu and Jenny's sense of abandonment and betrayal. Had I recognized that I was losing my balance, I could have remained present intellectually and emotionally.

Most conversations I had with my patients were much less emotional, even when I had bad news to impart. A discussion of recurrent hypercalcemia, for example, would not have been a "difficult conversation." There is nothing about hypercalcemia that triggers feelings in me of sadness, inadequacy, helplessness, or guilt, and nothing that triggers questions about my competence as a physician. But as a first-year oncology fellow, I was susceptible to all those feelings being triggered in me by the dilemma Yu presented. And that is probably why I dreaded having the conversation in that hospital room.

Now, as a palliative care physician, I'm better at recognizing these loaded conversations ahead of time. I ask patients and their families how they interpret the facts I give them, and explore how the case affects my own feelings and my sense of who I am. Now, before the encounter, I can prepare myself by talking over the facts and the feelings with colleagues.

The alternative, it seems to me, is simply to avoid the conversations that are just too painful. Or you may, unconsciously, strictly limit your emotional involvement with your patients. This lack of personal exploration into what makes a conversation difficult for you is likely to contribute to reluctance to share bad prognoses with patients who really need to know them. It is important to recognize how telling patients they have only weeks or months to live affects your emo-

tional equilibrium, and you need to understand how it can challenge your identity as a physician. Otherwise, the pain you experience at the thought of having these conversations may force you to abandon your patients when they need you most.

How to Break Bad News

Although we can become more skillful in breaking bad news, I don't want to suggest that even the most practiced delivery will diminish the effects on patients and their families. As Stone and colleagues put it (Stone et al. 2010, Introduction): "There is no such thing as a diplomatic hand grenade." Patients notice our body language, however, and delaying telling them is like "holding it after you've pulled the pin." Patients will notice our distress and may worry about the news, or worse, may worry that they have done something to anger or distress us.

Avoidance, therefore, is not a good strategy. But neither is what I call "truth dumping." I heard a terrible example of this one day as I walked to the cafeteria in the cancer center for lunch. A new oncology fellow was talking with one of his leukemia patients in the corridor leading to the cafeteria. She had come for blood counts and possibly a transfusion. The fellow knew the results of her recent bone marrow, however, and seeing her in the hallway, he felt compelled to tell her right there, in the entrance to the cafeteria, that her leukemia had relapsed. The poor patient was caught completely by surprise; she had not brought anyone with her because she hadn't expected to need any support; not surprisingly, she looked shocked, and she burst into tears. That conversation is what I mean by "truth dumping": the fellow dumped his distress at "carrying" the knowledge of the relapse onto the defenseless patient, without thinking of the potential consequences. He hadn't yet been taught how to break bad news, and this was the unfortunate result.

What makes breaking bad news hard to do, in most cases, is how you fear the patients will feel—about the news or about you, especially if you feel at some level that you should have prevented it. But if you can come to accept that what has happened to them is really not your fault, and that your job is to help your patients through this horrible thing that is happening to them, you will be able to tell them and to sit with them in their grief afterward. If you are able to listen for ways you can help them cope with their new status, you will be having what Stone and colleagues call "a learning conversation." They advise, "You may find you no longer have a message to deliver, but rather some information to share and some questions to ask." And that can feel much better.

When you master the basic components of delivering bad news skillfully and the components of the difficult conversation that I discussed earlier, your

patients will not be the only ones to benefit; you will, too. You will start to work within an intellectual framework that allows you to be emotionally open but not vulnerable or unprotected even when you have to break "really bad" news. You will understand the feelings and reactions welling up within you, their origins, and their true meanings. And most important, you will be much less likely to develop compassion fatigue, an emotionally crippling and painful disorder that commonly afflicts oncologists. (I discuss how to identify, prevent, and treat compassion fatigue in Chapter 4.)

But when I was a first-year fellow in hematology/oncology, long before I learned about how to break bad news, or to have difficult conversations, I had an experience I will never forget: the first time I had to tell someone I'd just met that she had acute leukemia. I was called to the emergency room one evening to see Miss Etta Brown.

"I'm All Right, Dear. Are You?"

Miss Brown was a 56-year-old woman who presented with a two-week history of profound weakness and the onset that day of a rash. The laboratory called me to review her peripheral blood smear, and I agreed that it contained the blast cells typically seen in patients with acute leukemia. Her rash was petechial, and she had no other symptoms or remarkable physical findings; but analysis of her marrow aspirate confirmed that she had acute myelogenous leukemia.

I was severely shaken by the implications of her diagnosis. But I composed myself, put on what I thought was my most cheerful face, then went into her hospital room and sat on her bed. I took her hand in mine and in my most encouraging manner said, *"I'm sorry, but your bone marrow test shows that you have a cancer in your bloodstream; we call it acute leukemia. It is causing your rash and your weakness. We have good treatment for it, though, and there is every chance you will go into a remission."*

My face must have belied my words, however, because she replied, with evident concern, *"I'm all right, dear. Are you?"*

Miss Brown had been sick for some time, she later told me. She was frightened because she could no longer walk to church without becoming very weak and short of breath. When the rash appeared, she was certain she was about to die, but she did not share her fear with me until *after* I had told her about the leukemia. My news actually came as a reprieve from an immediate death sentence, and she was greatly relieved. She now understood what was wrong and could prepare herself to fight it. She felt better that night, she said, than she had felt in a long time.

The reverse situation is probably more common—and more distressing. Mr. Alessio, for example, was a patient who had been admitted for pneumonia. I was called to consult when the team discovered that the infection was caused by an obstructing lung cancer. The reaction I got when I told him of his cancer was disbelief, denial, and intense anger.

At the time, I ascribed the difference in the two responses to the personalities of the patients. But subsequently, I found a more likely explanation in the book *How to Break Bad News: A Guide for Health Care Professionals,* by Dr. Robert Buckman, a medical oncologist (Buckman 1992). As he states, "The reactions of patients often depend on the gap between their expectations and what the physicians tell them." Miss Brown's expectations were, if anything, worse than the news I had given her, and she expressed relief. For Mr. Alessio, however, the gap was enormous, and his reaction was commensurate with his shock.

How to Break Bad News, as the title suggests, describes how to convey distressing information to patients and how to cope with their reactions. It delineates the principles that underlie these discussions and includes a step-by-step procedure to ensure that all important elements are detailed.

Dr. Buckman relates that he wrote the book after witnessing the following exchange (which I continue to hope is apocryphal). A urologist stood at the door of a hospital room, talking to two of his patients within. He said that both men could be discharged that day and that the results of their prostate biopsies were available. He told one man that his biopsy showed only inflammation. He then informed the other that his biopsy had shown cancer and suggested that he make an appointment to talk with him about it later that week. Then he left.

PRACTICE POINTS: BREAKING BAD NEWS

- Make yourself, the patient, and the family comfortable.
- Find out what they know.
- Find out what they want to know.
- Tell them in words they can understand, and in small chunks.
- Appreciate the role of silence.
- Respond to their feelings. Ask how you can help *now.*
- Ask them to summarize what you told them; ask whether they have further questions.
- Tell them the plan; let them know you expect further discussions as time goes on.

I cannot remember ever being quite that callous, but I am sure there were times when I did not plan the encounter carefully enough to minimize the effects of my news on the patient or his family.

Assembling the Team

How should we deliver bad news, and whom should we bring to the encounter with us? Suppose the roles were reversed: you just had a colon polyp removed. How would you want to get the pathology report? On the phone? In the office? Who would you want to have there with you? A family member? A trusted friend? Or, let's say you've just had restaging CT (computerized tomography) scans after a course of chemotherapy for ovarian cancer. Would you like the office nurse who has been giving your chemotherapy to be there when the physician tells you the results? The social worker who has been counseling you and your husband or partner? Each of us is likely to answer in a different way.

That is why it is so important to be sure the patient has a chance to think about this before the meeting takes place. With a little planning time, patients can usually arrange to have the right people with them. Whenever you schedule tests, you can ask patients to bring someone with them when they return for the results, so that when those results are problematic, patients will have the support they need. If you know the test results are bad, you can ask the relevant office personnel to free up time to be with you when you meet with the family, both to support you and to counsel the family when you need to move on to the next patient.

In the inpatient setting, ask the social worker to schedule the meeting at a time convenient for everyone who needs to be there, and to include whomever has been closely involved in the patient's care (e.g., the primary nurse, the chaplain). Be sure to ask the social worker to find a room in which everyone can be seated comfortably, rather than allowing the family and the rest of the team to stand while you and the patient are seated.

For the conversation itself, Dr. Buckman's book contains a number of useful, often commonsense suggestions, which I review in the sections that follow.*

Make Yourself, the Patient, and the Family Comfortable

With the team, the patient, and the family waiting for you at the meeting place, take a moment before you enter. Rehearse to yourself what you are about to say;

*Adapted from R. Buckman, *How to Break Bad News: A Guide for Health Care Professionals,* Baltimore: Johns Hopkins University Press, 1992.

try to dispel any feelings of guilt (which are almost always unwarranted), take a deep breath or two, and bring your full focus onto how you can be of most help to this patient and her family.

As you begin your encounter, use body language that indicates you have all the time in the world. This I learned from my brother, a gastroenterologist in private practice and a very busy guy. When accompanying him on follow-up visits, I noticed that he stretched out in a chair near the patient's bed or chair, looking as if he were camped out for the afternoon. He asked the questions he needed to ask, including open-ended ones, let the patients ask all they wanted, examined them, and then left. None of the encounters took more than about fifteen minutes, but as we left the patients seemed satisfied with the time my brother had spent with them.

Cancer patients also prefer their physicians to be sitting when they break bad news. In a randomized controlled trial using a video of a physician who was either standing or sitting while breaking bad news, patients (from a predominantly white U.S. population) considered physicians who were seated to be more compassionate (Bruera et al. 2007).

Find Out What They Know

After you and the family are comfortably settled, with a box of tissues close by, explore what the patient understands about what is wrong. You may know what the patient has been told by the house staff or by the surgeon who did the operation, but you need to determine what the patient remembers from those discussions and whether he understands the implications. You might say, "*The results of your tests finally came back, and I thought I would let you know what they are and what we're going to do about them. Of course, I will be answering any questions you have. But before I begin, it would help me to know what you already know and what you think is wrong with you.*"

Someone has usually told the patient that he has cancer and has explained its type, stage, and location before you, the oncologist, are asked to see him. Some of these patients, when asked what they think is wrong with them, repeat what they have been told, word for word. They also seem to understand the implications of their diagnosis. Others, given the same information by their own physicians, have said, "*They told me I have a tumor. You don't think that could be cancer, do you?*" This patient either hasn't understood what he was told (and was too embarrassed to admit this to his physician) or finds the implications too overwhelming. He may be in a state of denial, unable to accept that he could possibly have cancer. The discussion you have with him will be very different

from the one you can have with the first type of patient. For this second type, ask what he thinks a tumor is and what it means to him to have cancer. Follow his lead and try to allay any fears or correct any misconceptions that he reveals. But make it clear that he does have cancer and that you will be there to help him with all that is to come because of it.

Find Out What They Want to Know

Dr. Buckman counsels that we should next find out how patients want us to deliver the news and what they want to know. Dr. Diane Meier, professor of geriatrics and director of the Center to Advance Palliative Care at Mt. Sinai Medical Center, New York, suggests we try the following: "*In my experience, I have found that some patients want to know all the details each time I speak with them, while others would rather I described the big picture, leaving them free to ask for more details when they felt they needed them. In general, which would you prefer?*"

Next, having some idea of how broad or fine the strokes should be, find out more about the picture you've been commissioned to paint. Miss Brown, for example, asked me how long she had to live. This sounds like a fairly straightforward question—but so, on the face of it, does a child's question, "*Where do I come from?*" Many parents have responded to this by launching into a discussion of the birds and the bees, only to be met with perplexed looks and the complaint, "*I have to do a report for school on the city I come from. I just need to know if we come from Boston or San Francisco.*"

Miss Brown, it turned out, had tickets for a cruise in three months, and she wanted to know whether she was likely to be able to go on that cruise. She did not want to discuss her ultimate outcome. To approach patients' or family members' questions, therefore, ask them to be a little more specific about what they want to know and why they want to know it. You're more likely, that way, to know what question to answer.

Tell Them in Words They Can Understand, and in Small Chunks

Once you have a handle on the question, the next steps are similar to those you would use in any routine form of patient education. If you were explaining a chemotherapy regimen, a colonoscopy, or the fact that someone has an ulcer and needs to take certain medications, you would use words patients could understand and, when appropriate, visual aids.

When you are breaking bad news, however, you need to divide the information into smaller chunks. After the news sinks in that a person has cancer, she is unlikely to remember much else from that first talk. Some oncologists even advise letting patients record that first meeting on a phone or MP3 device, so that they can listen to it later, at their leisure.

How to Deal with the Response

The Role of Silence

At this point, stop talking for at least ten to twenty seconds. (To experience how long that is, slowly count to twenty silently. I think you'll find it takes much longer than you expect it to!) Both the quality of this silence and how you feel during it can vary. For those of you accustomed to silence from your own contemplative practice, you might be interested in enhancing the quality of this time with your patients by learning more about what Dr. Anthony (Tony) Back and his coauthors, all expert spiritual care practitioners, call "Compassionate Silence" (Back, Bauer-Wu et al. 2009).

These skilled practitioners can use this time in a special way. But for most practitioners, the first minute between when they deliver the news and when the patient or a family member says something can seem endless. As you sit there, if you are lightly touching the patient's hand or arm, be alert to a withdrawal of the limb, since contact may not be welcome then. But your silent presence is very important.

Patients who have just heard bad news are numb and shocked. It can take thirty to forty seconds for the information to sink in, for patients to replay internally what you've just said, and then to voice a thought or a feeling. The longer you let the silence last, the greater the chance they will have the time they need to process what you've told them.

While you wait for their response, take a moment to assess how you are feeling. If you feel anxious, relax, breathe "mindfully" (i.e., paying attention to each breath, as I discuss in Chapter 7), and check in visually for support from any of the colleagues you brought with you to the meeting, such as the nurse or nurse practitioner or social worker on your team, or the palliative care consultant.

Since you cannot control your patients' reactions, use the time instead to prepare yourself for their response, the next step in this "difficult conversation." You have delivered your version of the "facts," but prepare to be open to questions from the patient or family, who may have interpreted the same signs and symptoms and even radiology reports very differently from the way you interpreted

them. Remind yourself to be curious, and to try your best to be sure you ask enough questions so that you understand how they see things. Find out what they know that you don't, instead of assuming you know all you need to know. That will help you to guide them to the reality that you and your team see, and will help them move forward in the conversation.

Respond to Their Feelings

As I mentioned above, patients' reactions are likely to reflect the difference between their expectations and what they have just heard. Those who have been very ill or in pain yet have been told there is nothing wrong with them may, like Miss Brown, express relief that the source of their suffering has been identified. It is, naturally, much harder for those who have had no hint about the cancer.

Their first response may be verbal or nonverbal. Some reply with disbelief: "*You must be mistaken. The tests must have been mixed up in the lab. I feel fine. There can't be anything wrong with me.*" Others may look up at you in great pain, may cry, or may be totally silent. To the mute-stricken patient, rather than ask, "*How can we help?*" you might say, "*What do you need us to do* right now*?*" which calls for a more limited response. A patient might reply, "*Schedule the next tests you have to do as soon as possible. I can't wait much longer to find out how far this thing has spread.*" Or, "*Call my husband. He said he wanted to come with me, but I was so sure everything would be fine, I told him not to bother.*"

When the patient or family member is angry, wait out the storm. Families may express their anger at other physicians who have "missed the diagnosis," even if it was not apparent at the time of that consultation. Patients can be angry at you, or angry at their families for making them come to the doctor, or at God for allowing this to happen. If they are angry at you, use part of your consciousness to monitor your emotional response to their accusations. You'll be better able to guard again feelings of defensiveness if you have learned to recognize your own personal warning signs that you are in danger of losing your balance. In my case, I learned that I feel a tightness in my chest and dissociation from the situation. It's as though I'm there but not there. Now, when I sense that happening, I slow down or ask my colleagues in the meeting to contribute their thoughts so I can regroup.

Try to determine if the patient or the family member who is yelling at you might be doing that because they have lost their balance—if what you just told them caused such intense feelings or threatened aspects of their identity so profoundly that they cannot hold themselves together. If you suspect the problem is

with the other person's feelings or identity, you don't need to ask about that directly; just give them time and space, and they may find the way to get back to their best selves.

Your team members may be crucial if either you or the patient and family are overwhelmed by feelings or unbalanced by a threat to identity. When a young patient, Abigail, tearfully pleaded with her oncologist, "*You* can't *give up on me!*," the oncologist was struck dumb; we were able to help by assuring the patient that he would never give up, but that the burden of further treatment was so great that it was likely to shorten Abigail's life rather than buy the extra time she was asking him for. Her anger turned to a flood of tears, and we all supported them; the physician found his voice and was able to help Abigail and her family move forward.

Some patients turn the anger inward. They may not seem angry right after you tell them the news, but at later visits they may appear depressed or withdrawn. Some are blaming themselves for sins of omission or commission that they feel caused the cancer or delayed its diagnosis.

Have tissues within reach for the tearful patient, and try to offer some form of nonverbal support such as putting a hand on the patient's arm or shoulder. Speak reassuringly, making no attempt to stop the initial flow of tears, and, by making no effort to leave, indicate your willingness to be present no matter how emotional the patient becomes. The tears usually subside quickly, and you'll find you have established trust and a personal bond that will be helpful in the months or years to come.

To provide what Dr. Buckman would call an "empathic response" to a patient who is angry or crying, first identify the emotion, then ask questions that would help identify its source, and then say something to indicate you understand the connection between the emotion and its source.

Jason, a patient with prostate cancer, seemed to be blaming himself for developing the cancer. I said to him, *"I can really feel how angry you are. Why do you think you became ill?"* He responded, *"Well, I smoked, didn't I? And everyone knows that smoking causes cancer.*" I was tempted to correct Jason's misconception right away and to reassure him. But if I contradicted him, our conversation would have come to a close prematurely. Instead, I pursued the questioning, so that I could learn about all his sources of concern: *"And what else do you think contributed to your illness?"*

I did not know what he was going to say. He might tell me he hadn't gone to the doctor for years despite his wife's multiple urgings that he do so. He might report lapses in attendance at church services, failure to eat right, drinking too much alcohol—the list could go on and on. You never know what you're going to

hear. As I listened expectantly, Jason said that he had been having an affair and was furious with himself for being unfaithful to his wife, and that his cancer was a just punishment. He finished with, *"I guess that's about it."*

I was totally floored! But I replied, *"As I understand it, you're angry at yourself, and you're angry both because you feel your smoking caused your cancer and because you had an affair, for which you feel you deserve to be punished by getting prostate cancer. Is that right?"* I settled down, as did he. I felt I could now correct his misunderstanding about the relationship between smoking and prostate cancer. But I could also, if I had the time and the comfort level to do so, begin exploring with Jason issues of forgiveness and punishment. If not, I could express my sincere concern for his pain and explore whether he might seek help from a spiritual counselor.

Tell Them the Plan

Once patients have assimilated both the news and its implications for them, have had time to react, have shared their underlying concerns, and have had the opportunity to ask any remaining questions, you can move on to the plan, which usually includes further testing, referrals, or a chemotherapy regimen. Reassure patients that this is only the first of many discussions, and that your whole team will continue to answer their questions and provide or arrange for the support and counseling they or their family need. I often suggested that patients record all their questions in a notebook or keep an MP3 recorder nearby so that they won't forget to ask them at the next visit. I encouraged them to include questions from family or friends who were not at the meeting, but who are likely to raise additional concerns.

Ask Them to Summarize What You Told Them; Ask Whether They Have Further Questions

To bring this meeting to a close, you might say, *"I know we have gone over a lot of ground today. Since I may have used some technical terms that were unclear, it would help me if you would summarize for me what we've discussed."* Patients' answers, like their answers to the first questions about what they knew about their disease, will provide you with important information for your next visit. Despite your best efforts, you will find that some people are still unclear whether or not they even have cancer!

Most patients understand at least their diagnosis and the need for further tests. Remind them that you are available to answer their questions and those of

their family or friends and that you will be talking again later, as new information appears.

While it may seem longer, these talks usually take no more than fifteen to twenty minutes, though it's good to plan for a thirty-minute session. You can use the extra time to debrief with your nurse or social worker, review how they thought it went, and make plans for the next time you see the patient.

Provide Psychological Support

Often, the first time you meet patients is after they have just been told they have cancer. They are sometimes frightened, or numb, anxious to find out what will come next, or optimistic that they will be cured. Your first interview offers an excellent opportunity to begin psychological support, and you can offer that support even during the limited time of an office visit.

How? Expand the scope of your history of the disease, asking questions that reveal not just how the cancer was found, but also the emotional effects of the experience on the patient. The questions suggested by Faulkner and Maguire (1994), British experts in communicating with patients with cancer, are useful.

PRACTICE POINTS: ASSESSMENT OF NEW PATIENT

- Medical history
- Experiences seeking advice
- Effects of treatment
- Current state of the patient's disease and its effects
- Current psychological state
- Current mood state
- Overall level of functioning
- Other important life events

(From Faulkner and Maguire 1994)

Consider Joe Palermo, a 65-year-old man who has experienced symptoms of benign prostatic hypertrophy (BPH) for several years. Prostate specific antigen (PSA) levels were borderline during that time and were not elevated subsequently. On routine digital rectal exam, however, Joe's internist found a nodule that on biopsy proved to be cancer. Further studies indicated that the cancer had not spread beyond the prostate. Joe's internist referred him to Dr. Kew, the radiation oncologist, because Joe was interested in receiving radiation therapy rather than surgery.

In the course of a normal medical history, Dr. Kew would ask Joe how long he had had the symptoms of BPH, how troublesome they were, and when the nodule was discovered, and then would review the biopsy and staging studies with him. She would then explain the risks and benefits of the proposed radiation treatment.

This typical history, however, provides Dr. Kew with only the sketchiest view of Joe as a person who has to cope with this new cancer diagnosis and plan of treatment. She knows nothing of Joe's psychological state: how is he dealing with the diagnosis and the staging procedures? What are his fears and hopes, such as about having sex or remaining continent? Does he need more intensive psychosocial support during the planned therapy? To get to know the patient better, Faulkner and Maguire (1994) suggest the following to help explore these other areas.

Seeking advice. After the medical history, Dr. Kew should review with Joe his experiences seeking advice from physicians about his cancer. She might ask Joe whether he feels there were any delays in getting to the diagnosis (e.g., did he regret not having earlier studies done to evaluate his borderline PSA? Were they offered? Did he refuse them? How does he feel about refusing them?). Dr. Kew can also explore how Joe felt when his internist found the nodule, how he felt about the staging procedures, and what his concerns and hopes are now, as he anticipates the radiation treatment. What led him to the radiation therapist rather than back to the urologist who did the biopsy? Has anyone he knows ever gone through treatment for prostate cancer? What happened to them, and how does Joe feel about that?

Faulkner and Maguire suggest that, after the treatment begins, follow-up visits can be used to question more than just the physical side effects of the treatment. For example, Dr. Kew would normally question Joe about diarrhea, dysuria, skin changes, rectal pain, and fatigue, as well as do a complete review of systems. But in addition, consider how much more Dr. Kew will know if she also asks questions about other areas (Faulkner and Maguire 1994, pp. 36–42).

Effect of treatment. Typical questions to explore the effect of Joe's treatment would be (p. 36): "How has the treatment been affecting you? What has the effect been on your day-to-day life? Has it had any effect on your ability to continue working, and to maintain your normal social life, hobbies and interests?" Faulkner and Maguire also recommend asking questions that explore Joe's relationship with his partner (including their sexual relationship), his mood, and his ability to concentrate. Checking in on how the patient thinks things are going can help Dr. Kew dispel Joe's misconceptions and clarify the goals of the treatment.

Dr. Kew asks Joe and his wife, Bonnie, about how he is coping. Bonnie tells her that after three weeks of daily therapy, the reality of his cancer diagnosis has just

begun to sink in, and she thinks he has been having a great deal of difficulty dealing with the feelings that have begun to emerge. Joe reports that he has developed insomnia and a poor appetite; he admits to feelings of hopelessness and helplessness, and he no longer looks forward to things he used to enjoy, like playing poker with his friends.

Current psychological state. What is wrong? Joe may have just begun to face the psychological hurdles presented to patients newly diagnosed with cancer (pp. 1–6):

1. Uncertainty about the future: Will I be cured? How do I plan if I don't know how much time I will have?
2. The search for meaning: How do I make sense of what I have done during my life? Did I leave a mark? Will I be remembered?
3. Loss of control: Is there anything I can do to increase my chance of cure? What if there isn't?
4. The need for openness: Who should I tell? What will they think?
5. The need for emotional support: I don't want to be a burden. Do I have enough support from my friends or my family?
6. The need for medical support: Can I count on my oncologist? My primary care physician? What if there's nothing more they can offer?

If these questions remain unresolved, patients can develop chronic anxiety or depression. In fact, as I discuss in Chapter 9 the symptoms Joe is reporting, if they persist for more than six to eight weeks after the cancer diagnosis, would represent an adjustment disorder with anxiety or a depressed mood or even a major depression. By including in her assessment the questions that can reveal psychological distress, Dr. Kew will be able to refer Joe for the help he needs.

PRACTICE POINTS: PSYCHOLOGICAL HURDLES OF THE NEWLY DIAGNOSED CANCER PATIENT

- Uncertainty about the future
- The search for meaning
- Loss of control
- The need for openness
- The need for emotional support
- The need for medical support

(Adapted from Faulkner and Maguire 1994)

Overall level of functioning; other important life events. Receiving radiation therapy for prostate cancer is, of course, likely to cause a number of physical discomforts that might seriously interfere with Joe's ability to lead a normal life.

Joe began to need to defecate so frequently that at first he limited his trips away from home to places within two minutes of a restroom. A few weeks later, Bonnie says, he just stopped trying to leave home, giving up his poker group because he didn't want to explain to his friends why he wanted them to move the game permanently to his house. Bonnie is afraid that even if Joe is cured, the price he has paid will have been much too high. *"What use is living if it's going to be like this?"*

Dr. Kew could never have discovered Joe and Bonnie's misunderstanding about the permanence of the treatment-related changes if she hadn't explored how Joe's work was going and whether he had been keeping up with social activities. She now can offer treatment and help them make plans for when the side effects are likely to abate. Joe is less likely to develop a serious depression if he believes that he will soon return to his normal life.

Faulkner and Maguire caution, however, that the changes people report in their moods may be unrelated to their treatments. The real cause may be an unrelated problem, such as losing a job, or the serious illness or death of a close friend or relative. By pursuing the etiology of what you perceive as a significant personality or mood change in your patients, you are likely to uncover the true cause of the distress.

Delayed Presentation of Psychological Distress

Selina Basset, a patient I cared for when I still practiced oncology, also got bad news. But her response didn't occur during our first encounter; it happened later, when she was at home. Her distress was difficult to diagnose, because her delayed response manifested as signs and symptoms that are also found with known metabolic or other complications of her cancer.

Selina was then a 61-year-old corporate lawyer who visited her internist for unexplained weight loss and a cough she could not shake. Chest x-ray showed a mass near the right lung hilum, and she was referred to an interventional pulmonologist, who recommended a biopsy. Mrs. Basset requested a consultation with a medical oncologist before agreeing to the procedure, and I was able to see her later that same day.

After examining her, I reiterated her physicians' concern that the mass was likely to be cancerous and that it needed to be biopsied. She seemed to accept what I considered to be quite distressing news in a matter-of-fact way. She said she would agree

to the procedure, and she called later to inform me that she was having routine blood work done and staging scans, and that they were scheduled for the following Thursday. She had important work pending that she did not want to postpone.

The following Tuesday, however, I received a call from her husband, concerned because his wife was acting strangely: *"Selina asks the same questions over and over and seems not to pay attention to the answers, and she isn't sleeping much. What do you think is the matter?"*

I first wondered whether she could be hypercalcemic or have brain metastases but dismissed hypercalcemia as unlikely. After all, as recently as four days before, other than the weight loss, she'd had no abnormal physical or laboratory findings. Also, her husband did not report any other symptoms or signs that would support brain metastases.

It was more likely that Mrs. Basset was experiencing an acute anxiety reaction or an adjustment reaction that was causing her agitation. If the hilar mass proved to be cancer, she would be suddenly transformed from an independent, healthy, successful career woman into a "patient" with a possibly *fatal* condition. Although she had not discussed this fear with me, her internist, or her husband, it may well have precipitated her psychological distress, which would explain the behavior her husband described.

Patients like Mrs. Basset may respond to an anxiolytic agent such as lorazepam (Ativan) in the short term, but if they have not coped well with bad news in the past or do not have other sources of psychological support, they often benefit from working with a psychotherapist or a psychiatrist.

Therapists have a variety of important roles to play in helping patients and their families deal with the disease and its treatment. These roles include providing continuity of caring, being a knowledgeable advisor, and teaching valuable skills.

Therapists can provide the support a patient needs not only at the time of diagnosis but throughout the course of treatment. Many patients feel uncomfortable complaining to their oncologists. They do not want to seem to be "bad" patients; they cannot risk alienating your affections. It feels OK to complain to a therapist, who is someone with whom the patient can share disappointments and fears. The therapist can provide the continuity of caring many patients need to deal with the stresses of the disease and its treatment.

Therapists can also help a patient understand the cancer, its treatment, and the expected range of emotional and psychological responses. And they are often more aware than are patients, their families, or their friends of how effectively your oncology team can manage symptoms such as pain or nausea. They can

convince patients that it is safe (and important) to reveal their symptoms to you so that you can relieve them.

Finally, therapists can teach patients important skills to help them cope with cancer. Many therapists are trained in cognitive therapies such as mindfulness meditation or hypnotic techniques that help patients deal with depression, anxiety, and pain, as I discuss in more detail in Chapter 7. They can also teach patients a variety of coping strategies that will help them to reestablish a sense of control or to become more comfortable sharing that control with their oncology team or their families.

Mrs. Basset benefited from the lorazepam and welcomed the referral to a psychologist. She was found to have stage IV small cell lung cancer. She told me that the therapist had been an important source of support and information as she struggled to decide whether, since her cancer was not curable, she should even undergo what was likely to be very toxic therapy. Mrs. Basset said she felt freer to share with him certain concerns, rather than "bother" me, her husband, or her friends with such things. *"My idea of appropriate talk during a mah jong game,"* she said, *"doesn't extend to discussing how my sex life would change on chemotherapy."*

How to Raise the Subject of Advance Care Planning

You Need to Use the "D" Word

Mrs. Basset decided to take the chemotherapy. As she later told me, she had wanted to be sure that she would know that she'd done everything she could. If Selina did not take the treatments, she knew that she was much likelier to die sooner than if she did take them, and she, like many women her age, worried that her family would be thinking, "*Why didn't Mom just tough it out? Didn't she care enough about us to fight?*"

She discussed her decision not just with her family and her therapist but also with Monica Sloan, the nurse practitioner who co-practiced with her internist. Monica called me later to recount their conversation, which included her initiation of a discussion of advance care planning with Selina.

Monica's father had undergone chemotherapy for non–small cell lung cancer and during the treatment, when his resistance to infection was at its lowest, had developed such a severe pneumonia that he'd needed to be intubated and have his breathing supported by a respirator for several days. Therefore, although this was not a usual part of Monica's job, when Mrs. Basset told her she was planning to undergo chemotherapy for her lung cancer, Monica decided to broach the subject of advance care planning. Monica explained what advance

directives were and how a power of attorney for health care (a health proxy) could speak for Mrs. Basset if she were unable to express her own wishes.

Monica asked Mrs. Basset what her wishes were concerning resuscitation: "*I realized she is going to be in for a rough time, so I thought I should find out what her wishes are regarding resuscitation and being maintained on life support. Mrs. Basset seems to like to be in control, so I assumed she would want us to document her preferences, in case the chemotherapy caused a life-threatening complication. But I couldn't seem to get her to give me a straight answer.*"

I asked Monica what, exactly, she had asked Mrs. Basset. She replied, "*I asked her, 'Do you want everything done?' and she said, 'Of course.' So then I described the details of resuscitation and the various life-support measures, and Mrs. Basset said, 'I don't want any of that. My mother had a stroke, and our family was terribly traumatized watching her die. I don't want my own family to suffer like that.' I was confused, so I asked again, 'But you want everything done?' and she repeated 'Yes.' Mrs. Basset is usually so clear. How can she want two totally contradictory things?*"

She did not. Selina simply did not interpret Monica's questions in the same way Monica did. When asked if she wanted "everything done," Mrs. Basset probably thought she was being asked whether she wanted all possible measures taken to treat her cancer and support her through the chemotherapy. What Mrs. Basset did not understand was that she was being asked what she wanted done if she *died*. So I asked Monica, "*Did you use the 'D' word? Did you say, 'If you die, do you want us to resuscitate you? Once we have, do you understand that we will have to keep you on life-support machines for days or even weeks to preserve your life?'* "

Monica seemed rather shocked with the words I used but admitted she hadn't mentioned dying. I told her that, rather than asking "Do you want everything done?" which has a number of interpretations, I always used the "D" word. After all, I needed Mrs. Basset to focus on what she wanted done if she *died*. Even if she did not want to be resuscitated, she might find it acceptable to use life support for a period to recover from a complication. If, like Monica's father, she developed pneumonia, she might let us use ventilatory support for a week or two.

What if I could help Selina see what resuscitation was actually like? Preliminary data from a randomized controlled trial suggest that patients with advanced cancer who viewed a video of cardiopulmonary resuscitation being performed in addition to hearing a discussion of likely outcomes after CPR had a better understanding of CPR, and more chose not to have it performed than control patients who heard the same verbal discussion but did not view the video (Volandes et al. 2013).

Until videos like the one tested in the study above become widely available, you will be the one to explain what is likely to happen. And I don't think it makes sense to list for patients all the procedures we can perform, even if we explain them in

terms that patients and their families can understand. Dr. Steven Pantilat* shared with me a useful analogy that illustrates the problems with that approach.

He asked me to imagine that I was going to buy a computer for the first time, and that I encountered two different salespeople. He asked me to decide which person was more likely to be able to help me buy the computer that would best fit my needs.

Salesperson 1: *"How many Gigabytes of memory and how much RAM do you need? How many slots for stick drives? Do you use a cable or a wireless system? Is the computer going to be networked?"*
Salesperson 2: *"What do you want to use the computer for? Do you make presentations for talks and use videos or materials from other documents in the talks? Do you make your own videos? Do you need a lot of room for photographs?"*

Clearly, I hope we would all resemble Salesperson 2. We, too, have specialized knowledge and experiences that our patients are unlikely to share. And we have the advantage of knowing our patients over time, so that we can factor in their goals.

When I next saw Mrs. Basset, I was able to clarify her wishes. I probably said something like:

Selina, now that you are aware of the possible complications of chemotherapy, we need to discuss the possibility that they might cause you to become so desperately sick for a time that you would die if we didn't use machines to do the work that your own body is unable to do. You might need to be connected by a tube in your nose or throat to a respirator to help you breathe. Or if the worst happened, and you did die, would you want us to do everything we could to bring you back to life? That would include, in addition to that tube to make you breathe, CPR and shocking your heart to make it beat again.

Do you know anyone to whom that happened and who was then in an intensive care unit? Did you visit them? How did it make you feel? How do you think you would cope with something like that? How would you feel about not being able to talk with us? How would you feel about being dependent on that kind of a machine, in a bed in an intensive care type of setting?

If you needed that done to preserve your life, do you think you could live like that? For a while? For how long? Would it matter how well your cancer was responding to the treatment? What else would you want us to factor in? In addition to treating any

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pain or other symptoms you were experiencing, would there be something we could do to ease the experience for you, if you needed that machine to help you breathe, such as giving you earphones to help you listen to the music you like, or to have books read to you?

She did want everything done to treat her cancer, and she also wanted us to do whatever was necessary to *prevent* her from dying. She was even willing to allow intubation for a reversible condition. But if she *died*, given the extent of her cancer, she was *not* willing to be resuscitated, and she did not want to have her life prolonged by extraordinary measures. I then wanted to help her establish a formal health care proxy, and to complete the other advance care planning documentation, so I asked her:

Would you like more information on how to fill out a document that would instruct us in your wishes, or one that shows how to appoint someone to make the choices for you, who would be given your proxy, your power of attorney for health care? Would you like me to put your wishes into a medical order, a document that would be valid at any site where you'd be receiving health care?

Being a lawyer, she knew all about these and asked that I give her the standard forms to appoint a health care proxy. She and I also completed a Physician Orders for Life-Sustaining Treatment (POLST) form, which I will discuss later in this chapter. Other types of advance care planning forms are informative but do not include medical orders. They are useful in facilitating discussions among patients and their families, who can then share their decisions with you. One common form, *Five Wishes,* is available from Aging with Dignity (P.O. Box 1661, Tallahassee, FL 32302-1661; website: www.agingwithdignity.org). The cost is $5 per copy. Aging with Dignity has also developed a special form for adolescents and young adults that is available at the same website. It is titled, *Voicing My CHOICES*: *A Planning Guide for Adolescents and Young Adults*.

I praised Selina for having the courage to make these decisions and urged her to share them with her family, especially her husband, whom she wanted to appoint as her health care proxy. She demurred, saying she wanted him to be free to make whatever decisions he thought best for her at the time. But, since she liked "the facts," I told her that research showed that surrogate decision-makers, like her husband would be if she could not speak for herself, actually had less distress and felt less burdened if they clearly knew the patient's wishes (Wendler and Rid 2011).

Given her experiences with her mother, and the incurable nature of her cancer, I was not surprised by her decision to be allowed to die a natural death. But I was surprised by her next remark, and at the time I did not recognize the concern from

which it arose: *"I guess I won't be going to heaven, but at least I won't be putting my family through hell."*

The Patient with Spiritual Concerns

Years later, a Jesuit priest leading an ethics seminar explained the moral dilemma many Catholics like Mrs. Basset thought they faced if they refused to have their life maintained by artificial means: they assumed they were committing the moral equivalent of suicide and expected to be punished for this mortal sin. This hidden moral dilemma has caused many patients unnecessary anxiety.

The Catholic Church is, in fact, much more compassionate than that. In 1957, and reaffirmed in the original edition of the Catechism in 1994, and again in the second edition in 1997, the Church expressed its understanding that people who are dying are not expected to accept extreme measures to prolong their lives (Bradley 2009). Refusing to be resuscitated or to be kept alive by artificial means is acceptable to the Church; it is not a sin and is not considered suicide. As written again in the new edition of Catechism, "Discontinuing medical procedures that are burdensome, dangerous, extraordinary, or disproportionate to the expected outcome can be legitimate; it is the refusal of 'overzealous' treatment. Here one does not will to cause death; one's inability to impede it is merely accepted" (*Catechism of the Catholic Church* 1997, Subheading I, Respect for Human Life, 2278, 2279).

I wish I had known this when I was counseling Mrs. Basset. I could have answered her unasked question, eliminated the guilt she was feeling, and diminished her suffering. In fact, the teachings of Islam and of many Orthodox Jewish rabbis affirm the same principle: people with terminal illnesses are not required to endure unrelieved pain or suffering or to allow their lives to be prolonged by technological means. Some Orthodox rabbis and fundamentalist Islamic teachers, however, do not agree. Since all life is a gift from God, they reason, diminishing it by even one breath is morally unacceptable. For Buddhists, the question hinges more on the quality of the dying than on the death itself: the mind must be alert to do the work that needs to be done to prepare the soul for death and eventual rebirth. Therefore, the maintenance of life at all costs is not a priority.

Why Advance Care Planning Is So Difficult for Many Physicians

I was pleased that Monica had questioned Mrs. Basset about advance directives. Such discussions with people beginning intensive chemotherapy, or even with

those having far-advanced cancer, are by no means routine. In fact, when given a vignette that described meeting a new patient who had cancer that, even with treatment, carried a four- to six-month prognosis, one study found that only 30 percent of oncologists would discuss DNR status with that patient. About 20 percent said that they would discuss DNR only if the patient developed symptoms, and 10 percent would wait until there were no non-palliative treatments left (Keating et al. 2010). The findings of a large cohort study of over 2,000 patients with stage IV lung or colorectal cancer were similar: while three-quarters of the patients discussed end-of-life care with their oncologists, this discussion happened a median of only one month before they died, usually during a hospitalization (Mack, Cronin, Taback, et al. 2012).

You can enhance the chance that your patients will receive care that is in concert with their wishes, whether that be aggressive care or comfort care, if you discuss their wishes regarding end-of-life care (Mack et al. 2010). If you don't ask them, you may err on the side of providing unwanted, aggressive end-of-life care. Patients with advanced lung or colorectal cancer who had these discussions with their physicians were, in fact, *less* likely to receive aggressive care and more likely to use hospice services than patients who hadn't had those discussions (Mack, Cronin, Keating, et al. 2012).

Though I am now more comfortable with discussions about advance care plans, initially I had these discussions only to avoid being in the position of having an intubated patient look up at me accusingly and write on his Magic Slate, *"I never wanted to live like this. You told me about the other side effects of the chemotherapy, but you left this one out. Why didn't you ever ask me what I wanted?"*

WHY ARE PHYSICIANS RELUCTANT TO INITIATE ADVANCE CARE PLANNING DISCUSSIONS?

- Physicians are forced to face their own feelings about mortality.
- Physicians are loath to cause pain.
- Physicians feel guilty or are afraid of being blamed.
- Physicians assume they do not need to ask: they know their patients' wishes.
- Physicians feel impotent to prevent death and have not grieved their many losses. They have unrecognized compassion fatigue.

Luckily, that never actually happened to me. But the question remains: why is it so hard to bring up the subject? What feelings do these difficult conversations evoke? What effect do they have on our sense of self? According to the

literature, this reluctance to discuss advance care planning has many components, as discussed in the sections that follow.

Physicians Are Forced to Face Their Own Feelings about Mortality

Discussions about advance directives force us to ask ourselves how *we* would answer these questions, and many of us are not ready to face our own mortality. In my own case, I did not complete an advance directive or a document naming my power of attorney for health care until about twenty years ago. What prompted me was the combination of frequent travels from Philadelphia to New York City, the perils of the New Jersey Turnpike, and the New York law requiring clear, written documentation of my wishes should I become incapacitated. Since making my own arrangements, however, I noticed that, even when I still practiced as an oncologist, discussing advance care plans with my patients was easier than it had been before.

Physicians Are Loath to Cause Pain

Physicians are loath to cause pain, and discussions of mortality are at the least awkward and at the worst terrifying for patients and their families. The stress on the patient and on me, even in my palliative care role, is something I still have to brace myself for, every time.

Physicians Feel Guilty or Are Afraid of Being Blamed

By raising the possibility that a patient might die, you place yourself in what seem to be two contradictory positions—on the one hand, assuring patients that you will make them well, and on the other, reminding them that they are, after all, mortal. Patients who don't want to hear this may blame you for their vulnerability to death, and their anger at their disease may be transferred to you as the bearer of bad news. This fear of blame is one of the major impediments, Dr. Buckman says, to physicians' discussing advance directives with their patients.

Even when patients don't blame you, you may feel guilty, that it is your fault they are at risk of dying. I would wager that many physicians share with me an experience I had when I entered medical school: we were told that one in three of us would cause someone to come to harm because we had not worked hard in medical school and didn't know enough. Our errors of commission or omission might even kill someone. It is not surprising, then, that we are reluctant to bring up the subject of death.

Dr. Jerome Groopman, who cares for many patients dying of AIDS or cancer, states in his book *The Measure of Our Days* a sentiment I fear is shared by many physicians: "Although I knew that Matt was going to die, that everything had been done for him that could be done, *I still felt a deep sense of failure, of guilt* [italics mine]. We, his doctors, had failed Matt, unable to save his young life" (Groopman 1997, p. 110). Daniel Callahan, senior research scholar and president emeritus of the Hastings Center for Medical Ethics, explains that, as physicians, we are suffering from a delusion: that advances in medical technology will indefinitely postpone death. Any death, in that context, must be one for which we must accept the blame and the guilt (Callahan 1993).

Physicians Assume They Do Not Need to Ask; They Know Their Patients' Wishes

Some doctors may feel the discussion is unnecessary, that they know their patients well enough to be able to act on their wishes without ever directly asking them to complete an advance directive. Studies have indicated, however, that this assumption is incorrect (Downey et al. 2012). Physicians and families could not predict patients' wishes about treatments that would prolong life. Doctors chose for the patient what they would want for themselves, not what the patients, in separate questioning, said they preferred.

Physicians Feel Impotent to Prevent Death and Have Not Grieved Their Many Losses

Advance directive discussions may make physicians feel impotent; we are admitting that at some point there will be nothing more we can do to prolong the patient's life. During my first week as an intern, as I vividly recall, I encountered a physician who felt just this way. During sign-out rounds, the resident explained to us that one of the patients was expected to die. If that happened, the intern was to call and inform the family. When the resident left, I heard my colleague, who was on call that night, mutter to himself, "*No one is going to die on my shift!*" And no one did; he kept the patient alive until the next morning, when he would no longer be "responsible."

In their zeal to inspire us to study, our teachers told us that death is the enemy and that when someone dies, we have lost the battle. "*What patient,*" they implied, "*would choose a losing general to lead his army?*"

In my experience, however, most patients don't want any kind of general caring for them. They want someone who is knowledgeable, experienced, and

confident, but who can also be approached with questions and fears. They want physicians who know their own and medicine's limitations.

In fact, many patients are disturbed by the knowledge that, in this technological age, they can be kept alive in ways that are not acceptable to them. This knowledge is one of the underlying motivations for the movement toward legalizing assisted death. It is unlikely, then, that patients will lose faith in us or in medicine simply because we ask them to state their preferences about being resuscitated or being kept alive by artificial means.

Physicians Have Unrecognized Compassion Fatigue

For some of us, the problem may be unrecognized compassion fatigue. Compassion fatigue is the detachment and depersonalization that develops in therapists and others who care for people who have experienced extreme suffering such as torture or rape (Figley 1995). Physicians suffering from compassion fatigue are unlikely to be able to bear the additional pain that always accompanies a discussion of goals of care with a patient who is no longer responding to therapy. In the Self-Care section of Chapter 4, I discuss the factors that cause oncologists and palliative care clinicians, among others, to be susceptible to compassion fatigue and offer strategies for preventing and overcoming it.

When to Initiate an Advance Care Planning Discussion; What to Say

Although you may be ready to have these discussions, when is the best time? And what should you say?

More on Advance Care Planning

The "Near Miss"

The timing of the DNR (or DNAR: do not attempt resuscitation) discussion depends, of course, on a number of factors. For example, when I still practiced oncology, I found the following two new patients on my clinic schedule: Harry Bennett, a 65-year-old man with metastatic non–small cell lung cancer, and Mabel Reeves, a 65-year-old woman coming for adjuvant therapy for breast cancer. I felt much more pressure to have the talk with Harry than I did with Mabel, because I was less worried that something would happen to her before we had a chance to explore her goals and values.

As it happened, however, I neglected to have the discussion with Harry on that visit. Before his second visit with me, he was admitted to the intensive care

unit (ICU) for post-obstructive pneumonia. Although he was not intubated, he did require noninvasive positive pressure ventilation (BiPAP). While he recovered in the hospital, I decided to discuss with Harry and his wife, Gladys, his wishes regarding advance directives. I suggested, and they agreed, that he had had a "near miss." While I was hopeful that the radiation therapy would prevent a recurrence of this particular problem, he likely had less than a year to live, and we needed to talk about what would have happened had his respiratory status not improved.

The "near miss" had made clear to both of them how near Harry was to another respiratory decompensation, and they now understood much more clearly what life in the ICU would entail. Both Harry and Gladys were glad to review their options with me in the aftermath of the experience. Harry put it this way: "*That felt like a ride through the rapids and I was lucky to make it. I know my time might be shorter than I want it to be, and I need to think about whether I want to take the chance of continuing this ride if the river is likely to shoot me through them again.*"

To know how to advise Harry and Gladys, and to help them do useful advance care planning, I needed to know a lot about Harry. How informed did he want to be about his condition? What did he understand of his prognosis? What was important to him in his life? What made his life worth living, and what would be unacceptable to him? If Harry got sicker, which goals were most important to him: longevity at all costs, comfort, independence? How much was he willing to endure for these goals? What did he fear losing, and what level of function would and would not be acceptable? What were his worries about Gladys and the rest of his family, his job, and other aspects of his emotional, social, spiritual, and physical life? How much did his family or Gladys, his health care proxy, know about his wishes?

I knew, as Harry and Gladys could not, what CPR or life on a ventilator, in a coma, or as a quadriplegic might entail, and I needed to help them make choices to ensure that his life, even if limited by illness or injury, would have quality for him.

Answers to those questions are most important for patients like Harry, whom you expect to live only a matter of months or a year. They are also important for those who have not responded to first- or second-line therapy, or whom you expect to have relatively refractory disease. Answers will become clear from conversations with you, your nurses or nurse practitioners, or the social workers in your practice. Ideally, your electronic medical or health record will have a place to record these conversations over time. We are developing such a module that is populated with typical answers in all those domains as well as allowing free-form text in an "other" box. When answers change, as they often do when a patient's disease and disability progress, we hope that soon, all the clinicians caring for patients in the outpatient setting, emergency departments, hospitals,

rehabilitation hospitals, or nursing homes that are part of our health system will have access to the module and be able to enter updates.

Knowing the answers to these questions will help you advise your patients on the burdens and benefits to them, personally, of CPR when they die. In the above scenario, Harry's previous experience with chemotherapy and its side effects were the springboard for the discussion. Those of you who care for patients with equally dismal prognoses (e.g., in the end stages of lung disease, heart failure, or cirrhosis), with whom it is equally important to do advance care planning, might use the seriousness of these diseases for your springboard:

Mrs. Elliot, you know we have discussed on many occasions how far advanced your lung disease is. I am glad that you feel so well today, and I plan to continue this regimen as it seems very effective. However, given the seriousness of your underlying condition, there is something important we need to discuss.

PRACTICE POINTS: DISCUSSING ADVANCE CARE PLANNING

- Initiate the discussion with patients early in the relationship.
- Discover who they want to have with them when you have the discussion, ideally their healthcare proxy.
- Anticipate and address unasked questions.
- Find out what makes this patient's life worthwhile, as well as what would be completely unacceptable, what she is hoping for, and what she fears.
- Reassure patients that having this discussion does not mean that you think the treatment will not work.
- Clarify the difference between taking measures to prevent death and taking measures to restart and sustain life once a cardiac or respiratory arrest has occurred.
- Ask specifically about patients' wishes regarding resuscitation should they die, and the expectations about what life would be like after the resuscitation attempt.
- Correct unrealistic expectations and misconceptions about the process and likely sequelae of resuscitation and about the experience of being kept alive by a respirator.
- Discuss the utility and limitations of a durable power of attorney for health care, living wills, and other written advance directives for health care.
- Encourage patients who are undecided at the initial encounter to discuss the subject with you again at later visits.

It is also very important to clarify patients' wishes about being intubated, not as part of a resuscitation but to prevent them from dying. As was true in Mrs. Basset's case, many people who do not want to be resuscitated if they die would be willing to receive respiratory support for a time to allow them to recover from a reversible process. I therefore include a discussion such as this:

I also need to understand how you feel about being kept alive on a breathing machine. The treatments are very likely to decrease your resistance to infection, and you might develop a serious pneumonia. While you were recovering you might need a breathing tube and a machine called a respirator to help you breathe. You wouldn't be able to eat or to talk, but you'd be able to communicate with us in other ways. Would that be OK with you?

Because many patients are worried about having their lives prolonged by these machines, I also add, *"I would never use a breathing machine to prolong your suffering, though. If it looked as if you were so seriously ill that the respirator was no longer helping you achieve any of your goals, and was merely keeping you alive, we would help you to die naturally and peacefully."*

Over half the patients I talk to about this in my role as palliative care consultant have an answer ready the first time I ask them. Others often stop me before I get very far into the discussion, saying that if their time has come they want to be left in peace. In fact, patients seem much less reticent to discuss these issues with me than I had ever imagined. When I have had such conversations in the hospital with a newly referred patient, the patient in the next bed has often volunteered his own wishes about resuscitation. A number have even asked, *"Would you tell my doc for me, doc? She seems to change the subject every time I try to bring it up."*

Discussing Prognosis

Your patients and their families cannot really engage in a meaningful discussion of resuscitation and mechanical life support until they have a realistic understanding of their prognosis. Prognosis, however, is shrouded in uncertainty, and the natural tendency when confronted with uncertainty about such an important subject is to avoid the discussion altogether (Levy 1999).

Further, the cultural "norms" of medicine dictate that we be optimistic rather than accurate (Christakis 1999). Of 700 oncologists (64 percent of the 1,100 ASCO members initially queried) who completed a self-report survey, over 98 percent replied that they told their terminally ill patients that they

would die. But almost half (48 percent) said that they only did so when patients specifically asked for information about their prognosis. Fifty-seven percent said they "sometimes, rarely, or never" gave an actual estimate of how much time the patient was likely to survive (Daugherty and Hlubocky 2008).

In a separate study, 60 percent of medical oncologists reported that they would rather not talk about advance directives, code status, or hospice until no more effective treatments remained (Keating et al. 2010). Delaying this long may leave patients less able to participate fully in the discussion or in decision-making. Executive function, which involves planning, insight, abstraction, and judgment, is impaired in patients with serious chronic medical illnesses like hypertension, COPD, and diabetes (Schillerstrom et al. 2005) and is likely therefore to be impaired in patients with advanced cancer. If you need to check formally for decision-making capacity in such a patient, without co-morbid psychiatric conditions, several instruments are available (Sessums et al. 2011).

In addition to feeling that we need to be optimistic about delivering a patient's prognosis, why else might we resist having the discussion? Drs. Jenny Mack and Thomas Smith, both oncologists, identified four more possible concerns:

1. Patients get depressed
2. The truth kills hope
3. Hospice or palliative care reduces survival
4. This talk is not culturally appropriate

But the data don't support these concerns (Mack and Smith 2012).

PRACTICE POINTS: WHAT DISCUSSIONS OF PROGNOSIS WON'T DO

- Depress patients
- Take away hope
- Reduce survival
- Be completely inaccurate
- Be culturally inappropriate

Patients don't get more depressed. Data actually indicate that patients who reported having end-of-life discussions did not have a higher rate of depression. In fact, almost 90 percent of 988 patients who were thought by their physicians to have six months or less to live, who were interviewed about death, dying, and bereavement, reported no stress at all after the interview; only about 2

percent reported experiencing a great deal of stress (Emanuel et al. 2004). Their caregivers reported similar remarkably low levels of stress, and about half of each group found the conversation helpful. Not having the discussion, however, is likely to lead to worse outcomes for the bereaved family. Patients who don't have those discussions are more likely to have more aggressive care at the end of life, and their bereaved caregivers are more depressed (Wright et al. 2008).

The truth doesn't kill hope. Both patients themselves and the parents of pediatric patients maintained hope even when they were told of a poor prognosis, low likelihood of response to treatment, or no chance of a cure (Mack and Smith 2012). In a small study of adult cancer patients, hope (as measured by the Herth Hope Index) did not change when patients were given truthful information by their oncologists about a bad prognosis (Smith et al. 2010). And 93 percent of surrogate decision-makers for critically ill ventilated patients also agreed that they would not want to avoid discussions of prognosis just to maintain "hope." Rather, they wanted accurate estimates of how long the patient was likely to live so that they could support the patient and be able to prepare themselves for what lay ahead (Apatira et al. 2008).

Neither hospice nor palliative care decreases survival. Patients in a hospice program do not have reduced survival rates (Connor et al. 2007), and in patients with advanced lung cancer about to begin chemotherapy for it, palliative care actually increased survival (Temel et al. 2010; Smith et al. 2012).

The talk is often appropriate across cultures. Although there is no "one size fits all" discussion for each person in a given culture or ethnic group, *it is not true that this subject is never culturally appropriate*. In general, patients from various ethnic and cultural backgrounds differ in what their preferences are for information, the ideas of each individual patient need to be explored. As Mack and Smith (2012) note, about two-thirds of European Americans and African Americans report that they want to be told about a terminal prognosis, as opposed to about half of Mexican Americans and about a third of Korean Americans, but these numbers allow for a large amount of individual variability. And these differences extend to completing advance care plans. Only 47 percent of black and Hispanic patients, compared with 80 percent of white patients, had an advance care plan (Smith et al. 2008).

Many patients want their families involved in the decision process and may even want the family to make the decision. Korean Americans and Mexican Americans, in general, are more likely to want this compared with patients from non-Hispanic white or black descent (Searight and Gafford 2005). Among Asians, the illness is also likely to be considered a family affair. Some patients

from Chinese, Pakistani, Bosnian, Native American, Filipino, or Italian American cultures do not want direct disclosure to the patient because such disclosures are felt to be self-fulfilling. Members of Asian, Bosnian, and Italian American cultures might perceive frank communication about a serious illness or prognosis as "at a minimum, disrespectful, and more significantly, inhumane" (Searight and Gafford 2005, p. 517). It is therefore important to determine from the patient whether her designees are to be involved in these discussions and to respect that choice as the exercise of that patient's autonomy.

You might assume that patients who want to know their prognosis will ask you about it. There are no data, however, on how often patients with cancer do ask about their prognosis. In fact, patients are known to withhold other concerns from their oncologists because they want to be "good patients" and "fighters," not "quitters." As I discuss in Chapter 5, patients often don't tell you about their unrelieved pain, and only about 15 percent of them volunteer the information that they have completed an advance directive (Lamont and Siegler 2000), thereby saving us the pain of this talk altogether!

Clearly, discussing prognosis does not fit easily into a standard office visit and requires skills that your medical training was unlikely to develop (Yuen et al. 2011). Only when I began to practice palliative medicine did I learn the skills I would have needed to discuss prognosis well with my patients and their families, such as how to run a family meeting, counsel patients in psychological distress, and help people cope with their grief and anger (Tulsky et al. 1995; von Gunten et al. 2000; Back, Arnold et al. 2009). Those of you who have not been adequately prepared for these tasks may decide not to mention prognosis for fear of harming patients or family members through lack of expertise.

Whatever your skills in these areas, however, it is particularly important to have a discussion of prognosis with a patient who still has a relatively good performance status, but who is likely to have only months left to live. Patients will make different choices about resuscitation if they know what you know, both in terms of their prognosis and of the likely functional or cognitive impairment resulting from resuscitation (Fried et al. 2002). Patients who reported that they knew their disease was terminal (or who had a discussion about end-of-life issues with their physicians) were much less likely to want life-extending care than were others (Wright et al. 2010).

And the data overwhelmingly suggest that resuscitation of these patients usually has a terrible outcome. A meta-analysis reviewed forty-two studies of resuscitation of inpatients with cancer between 1966 and 2005. It did not matter whether the patient was receiving cancer-directed therapy or palliative care

only—patients with cancer who arrested in the ICU or who had metastatic cancer and a poor performance status (KPS of ≤50) had only a 2.2 percent chance of survival. Patients with localized cancer had a 9.5 percent chance of surviving CPR, and those with metastatic cancer and KPS >50 had a 17.5 percent chance. As many as 45 percent of these patients were successfully resuscitated in the hospital, *but only one in ten of them survived to discharge.* Most of the studies did not report morbidity or place of discharge, but those that did reported that patients were often severely mentally incapacitated, and almost none went home. Sharing this information with patients is likely to help them make more informed decisions about being resuscitated, especially if their idea of what is likely to happen to them if they're resuscitated is based on what they have seen on television.

Looking at it another way, patients will elect to be resuscitated unless they think their disease is so far advanced that they have a very small chance of surviving a year. Patients who thought they had a more than 10 percent chance of surviving six months, for example, usually wanted to be resuscitated. Only patients who thought they had a less than 10 percent chance of surviving six months overwhelmingly chose comfort care and did not want to be resuscitated (Weeks et al. 1998). But this was not true for black or Hispanic Americans, both of whom were more likely to want life-prolonging care even with only days left to live (black, 45 percent of patients; Hispanic, 34 percent; and white, 14 percent; Smith et al. 2008). Not surprisingly, medical costs in the last six months of life are higher for these patients (Kelley et al. 2011), and it can be challenging to care for them, because the medical team is often at odds with them and their families (Quill et al. 2009; Jecker and Schneiderman 1995). You will likely need the strategies I discuss later in the chapter, when I review how to deal with conflict in advance care planning.

Just because a patient has far-advanced disease, you cannot assume that he has realistic expectations of chemotherapy. A recent study of more than 1,000 patients with newly diagnosed stage IV lung or colorectal cancer revealed that 69 percent of patients with lung cancer and 81 percent of patients with colorectal cancer "did not report understanding that the chemotherapy was not at all likely to cure their cancer" (Weeks et al. 2012).

When patients or their families seem unrealistic about the prognosis, try very hard to integrate information about their prognosis into the discussion about advance directives. Patients who have been resuscitated for an uncomplicated cardiac arrhythmia in the past and have gone home with no sequelae, or who have a close relative or friend who has been successfully resuscitated without serious sequelae, are particularly likely to want resuscitation. It is much

harder for them to understand that having metastatic cancer greatly reduces their chances of being successfully resuscitated and being able to return home from the hospital after a cardiac arrest.

You might say something like the following, stopping to deal with the patient's comments as they occur:

As we discussed before, your cancer has spread. We will be doing everything we can to help you maintain an active and fulfilling life for as long as possible. As we go along, you'll decide, as you always have, which treatments are worth the trouble. And I will let you know, as I always have, what the chances are that the treatment will be of benefit to you.

I will, however, need you to tell me soon how you feel about some extreme treatments we would use only if you died, like restarting your heart should it stop. Or, if you couldn't breathe on your own, how would you feel about us keeping you alive on a breathing machine? I feel fairly confident that you or your family have thought about this a little already; you might even have discussed it among yourselves—or you may have been afraid to bring it up because you didn't want to hurt each other.

It's important for you to take into account, while you're making your decision, what the outcome is likely to be if you die and we do resuscitate you. I would imagine that you're thinking, "Well, if I die in the hospital, of course I want to be resuscitated so that I can go back home." *Unfortunately, while there is a very good chance we could restart your heart, there is really almost no chance that you would get well enough to go home. I know that seems hard to believe, but it's true, and I knew you would want to know this to help you decide.*

Documentation of Advance Care Plans

Once you and your patient have defined the advance care plan, it's important to document it. You or one of your partners or nurse practitioners may at some point need to work with the patients' surrogate decision-makers (their health care proxies) rather than the patients themselves if the patient is so ill that she can no longer choose for herself (Silveira et al. 2010). If there has been an end-of-life discussion and an advance care plan made, patients, at least the elderly ones, as studied, are likely to have their preferences honored (Silveira et al. 2010; Detering et al. 2010).

Ideally, you will be able to record the advance care plan somewhere that is accessible not only to colleagues in your practice but also to Emergency Department and inpatient physicians in your usual referral hospitals, and to rehabilitation and nursing home personnel, if that's relevant. It would be helpful if Electronic

Medical / Health Records had a standard site to record this information, but many do not, or if they do, it is not accessible outside a single practice or institution. As I mentioned earlier in this chapter, we are working on a comprehensive electronic document that records much more than resuscitation preferences.

POLST and MOLST Forms

Although many clinicians currently lack that electronic capability, if you have a patient with a life expectancy of a year or two who wants to limit life-sustaining therapies, both the POLST (Physician Orders for Life-Sustaining Treatment) and its adapted form, the MOLST (Medical Orders for Life-Sustaining Treatment), promise to be a major step forward in comunicating this choice to all caregivers and emergency personnel (Meier and Beresford 2009) (Figure 1.1 and http://www.cdph.ca.gov/programs/LnC/Documents/MDS30-ApprovedPOLSTForm.pdf). POLST and MOLST forms are not supposed to replace health care proxy forms or living wills; rather, each is a two-page set of *medical orders* signed by the patient's physician, nurse practitioner, or physician assistant. These orders specify the patient's choices for cardiopulmonary resuscitation and medical interventions (directed at comfort, at full treatment, or at limited treatment); when or if the patient wishes to be transferred to a hospital or to an intensive care unit; and when or if the patient wishes to receive antibiotics, artificial nutrition, or hydration.

POLST and MOLST forms are legally valid for care *across all settings*, including the home, nursing homes, and acute care hospitals (Meier and Beresford 2009). The National Quality Forum endorsed the POLST as part of a health care system's quality standards in end-of-life care. The POLST was used first in 1991 in Oregon. As of September 2012, either it had been adopted or a program was in development in all but twelve of the fifty states. The forms were adopted by California, Colorado, Delaware, Hawaii, Idaho, Louisiana, Massachusetts (uses the MOLST form), Montana, New York (uses the MOLST form), North Carolina, Oregon, Pennsylvania, Tennessee, Utah, Washington, and West Virginia; and a program was in development in Alabama, Alaska, Arizona, Connecticut, Florida, Georgia, Illinois, Indiana, Iowa, Kentucky, Maine, Michigan, Nebraska, New Hampshire, New Jersey, New Mexico, Ohio, Rhode Island, South Carolina, Texas, Vermont, and Virginia. I urge those of you who work in states in which the forms have been adopted to become familiar with them, keep a stack in your office, and complete them as you have the discussions with your patients and their families. Copies are as valid as the original, so you can keep the original in your files or scan it into your electronic medical record and give copies to patients to keep with them in the car and at home.

SEND FORM WITH PERSON WHENEVER TRANSFERRED OR DISCHARGED
To follow these orders, an EMS provider must have an order from his/her medical command physician

pennsylvania
DEPARTMENT OF HEALTH

Pennsylvania Orders for Life-Sustaining Treatment (POLST)

Last Name

First/Middle Initial

Date of Birth

FIRST follow these orders, **THEN** contact physician, certified registered nurse practitioner or physician assistant. This is an Order Sheet based on the person's medical condition and wishes at the time the orders were issued. Everyone shall be treated with dignity and respect.

A Check One

CARDIOPULMONARY RESUSCITATION (CPR): Person has no pulse and is not breathing.

☐ CPR/Attempt Resuscitation ☐ DNR/Do Not Attempt Resuscitation (Allow Natural Death)

When not in cardiopulmonary arrest, follow orders in **B**, **C** and **D**.

B Check One

MEDICAL INTERVENTIONS: Person has pulse and/or is breathing.

☐ **COMFORT MEASURES ONLY** Use medication by any route, positioning, wound care and other measures to relieve pain and suffering. Use oxygen, oral suction and manual treatment of airway obstruction as needed for comfort. ***Do not transfer*** *to hospital for life-sustaining treatment.* ***Transfer*** *if comfort needs cannot be met in current location.*

☐ **LIMITED ADDITIONAL INTERVENTIONS** Includes care described above. Use medical treatment, IV fluids and cardiac monitor as indicated. Do not use intubation, advanced airway interventions, or mechanical ventilation.

Transfer *to hospital if indicated. Avoid intensive care if possible.*

☐ **FULL TREATMENT** Includes care described above. Use intubation, advanced airway interventions, mechanical ventilation, and cardioversion as indicated.

Transfer *to hospital if indicated. Includes intensive care.*

Additional Orders _____

SAMPLE

C Check One

ANTIBIOTICS:

☐ No antibiotics. Use other measures to relieve symptoms.

☐ Determine use or limitation of antibiotics when infection occurs, with comfort as goal

☐ Use antibiotics if life can be prolonged

Additional Orders

D Check One

ARTIFICIALLY ADMINISTERED HYDRATION / NUTRITION:
Always offer food and liquids by mouth if feasible

☐ No hydration and artificial nutrition by tube.

☐ Trial period of artificial hydration and nutrition by tube.

☐ Long-term artificial hydration and nutrition by tube.

Additional Orders

E Check One

SUMMARY OF GOALS, MEDICAL CONDITION AND SIGNATURES:

Discussed with
☐ Patient
☐ Parent of Minor
☐ Health Care Agent
☐ Health Care Representative
☐ Court-Appointed Guardian
☐ Other:

Patient Goals/Medical Condition:

By signing this form, I acknowledge that this request regarding resuscitative measures is consistent with the known desires of, and in the best interest of, the individual who is the subject of the form.

Physician /PA/CRNP Printed Name:	Physician /PA/CRNP Phone Number
Physician/PA/CRNP Signature (Required):	DATE

Signature of Patient or Surrogate

Signature (required)	Name (print)	Relationship (write "self" if patient)

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Figure 1.1. Sample POLST form, used in Pennsylvania (Pennsylvania Orders for Life-Sustaining Treatment), www.upmc.com/Services/AgingInstitute/partnerships-and-collaborations/Documents/POLST-Form.pdf.

SEND FORM WITH PERSON WHENEVER TRANSFERRED OR DISCHARGED

Other Contact Information

Surrogate	Relationship	Phone Number	
Health Care Professional Preparing Form	Preparer Title	Phone Number	Date Prepared

Directions for Healthcare Professionals

Any individual for whom a Pennsylvania Order for Life-Sustaining Treatment form is completed should ideally have an advance health care directive that provides instructions for the individual's health care and appoints an agent to make medical decisions whenever the patient is unable to make or communicate a healthcare decision. If the patient wants a DNR Order issued in section "A", the physician/PA/CRNP should discuss the issuance of an Out-of-Hospital DNR order, if the individual is eligible, to assure that an EMS provider can honor his/her wishes. Contact the Pennsylvania Department of Aging for information about sample forms for advance health care directives. Contact the Pennsylvania Department of Health, Bureau of EMS, for information about Out-of Hospital Do-Not-Resuscitate orders, bracelets and necklaces. POLST forms may be obtained online from the Pennsylvania Department of Health. www.health.state.pa.us

Completing POLST

Must be completed by a health care professional based on patient preferences and medical indications or decisions by the patient or a surrogate. This document refers to the person for whom the orders are issued as the "individual" or "patient" and refers to any other person authorized to make healthcare decisions for the patient covered by this document as the "surrogate."

At the time a POLST is completed, any current advance directive, if available, must be reviewed.

Must be signed by a physician/PA/CRNP and patient/surrogate to be valid. Verbal orders are acceptable with follow-up signature by physician/PA/CRNP in accordance with facility/community policy. A person designated by the patient or surrogate may document the patient's or surrogate's agreement. Use of original form is strongly encouraged. Photocopies and Faxes of signed POLST forms should be respected where necessary

SAMPLE

Using POLST

If a person's condition changes and time permits, the patient or surrogate must be contacted to assure that the POLST is updated as appropriate.

If any section is not completed, then the healthcare provider should follow other appropriate methods to determine treatment.

An automated external defibrillator (AED) should not be used on a person who has chosen "Do Not Attempt Resuscitation"

Oral fluids and nutrition must always be offered if medically feasible.

When comfort cannot be achieved in the current setting, the person, including someone with "comfort measures only," should be transferred to a setting able to provide comfort (e.g., treatment of a hip fracture).

A person who chooses either "comfort measures only" or "limited additional interventions" may not require transfer or referral to a facility with a higher level of care.

An IV medication to enhance comfort may be appropriate for a person who has chosen "Comfort Measures Only."

Treatment of dehydration is a measure which may prolong life. A person who desires IV fluids should indicate "Limited Additional Interventions" or "Full Treatment.

A patient with or without capacity or the surrogate who gave consent to this order or who is otherwise specifically authorized to do so, can revoke consent to any part of this order providing for the withholding or withdrawal of life-sustaining treatment, at any time, and request alternative treatment.

Review

This form should be reviewed periodically (consider at least annually) and a new form completed if necessary when:
(1) The person is transferred from one care setting or care level to another, or
(2) There is a substantial change in the person's health status, or
(3) The person's treatment preferences change.

Revoking POLST

If the POLST becomes invalid or is replaced by an updated version, draw a line through sections A through E of the invalid POLST, write "VOID" in large letters across the form, and sign and date the form.

How to Discuss Advance Care Planning with the Patient's Family: What Works and What Doesn't

I have discussed how to talk with patients and their families about advance care planning, both those who have and have not experienced resuscitation attempts. Even more difficult situations arise with patients on life support who have not told you their advance care plans, have not given you any advance directive forms, and have not discussed with you their wishes about artificial life support or resuscitation. You are then forced to discuss these issues with family members or partners whom you may or may not have met. The experiences I had with the families of Mr. Madison and Mr. Jordan illustrate many of the problems that arise in such situations, and the techniques for addressing them. The advice on holding family meetings in these situations, which was offered in the book *Mastering Communication with Seriously Ill Patients* (Back, Arnold, et al. 2009), based in part on Buckman, *How to Break Bad News* (1992), was key. The steps we included were:

1. Hold a pre-meeting with all the patient's health care providers to establish consensus on "best choices" and identify family decision-maker(s). Ensure that key personnel can be present for the meeting, including someone who knows the current medical details and, ideally, someone from the outpatient team who has a longitudinal relationship with the patient and family.
2. Find a site and a seat for all participants.
3. Ask the family to review with you how they think the patient is doing and what they see as the problems.
4. Ask the family what they think is likely to happen.
5. Ask the family what they hope and fear will happen.
6. Let each person who wishes to speak do so.
7. Explain the patient's current medical condition in global terms first, using lay language, and clarify the current prognosis; put any details of how each "system" is doing into the overall context of how the whole patient is doing.
8. Answer questions about the medical condition, using lay language; check for understanding frequently.
9. Ask the family again, in light of this new information, what they hope and fear will happen.
10. Delineate any key differences in priorities among the patient, health proxy, and medical care team.
11. Explain to the family what is possible and what is likely.

12. Work to achieve consensus.
13. Document the personnel present, key information gained, and next steps (Back, Arnold, et al. 2009; Buckman 1992).

Cultural Considerations

The cultural and ethnic backgrounds of your patients and their families clearly inform their views about how to do advance care planning and what care at the end of life should entail (Searight and Gafford 2005). Non-Hispanic whites and African Americans, for example, differ in whom they want present: non-Hispanic whites want immediate family only, while African Americans want their extended family, friends, and pastor. Non-Hispanic whites more often want to have a durable power of attorney or living will in place and are more interested in knowing about hospice programs than African Americans (Searight and Gafford 2005; Hwang et al. 2003; Phipps et al. 2003).

They also differ in what the focus and tempo of the discussion should be. Non-Hispanic whites want a focus on their concerns about prognosis, irreversibility of the illness, quality of life, financial concerns, and medical choices. African Americans, in contrast, favor a focus on spiritual concerns, lack of trust, concerns about "do not resuscitate" orders and hospice, and having adequate time allowed for decisions, without pressure to make them (Phipps et al. 2003; Shrank et al. 2005).

When the clinician is not a fluent speaker of the patient's language, every effort should be made to provide a qualified translator in conversations about prognosis and goals of care (Searight and Gafford 2005). Translators do not simply translate; they can explore whether the patient and family align with the usual cultural norms of their ethnic and cultural group, advise the team what those norms are, and alert them when a relevant cultural belief is likely to affect the discussion, such as telling a patient of the Islamic faith that he has a terminal illness (Butow et al. 2010).

A full discussion of the effects of culture on communication is beyond the scope of this book. For those readers who wish to pursue this subject in greater detail, I recommend the work of Marjorie Kagawa-Singer and Shaheen Kassim-Lakha, who have written extensively on the role of cultural differences in health care. I have included in the bibliography an article that discusses, ". . . an anthropological perspective of the fundamental relationship between culture and health, and . . . systemic changes needed within the social and legal structures of our health care system to reduce the risk of cross-cultural miscommunication and increase the likelihood of improving health outcomes for all populations within our multicultural US society" (Kagawa-Singer and Kassim-Lakha 2003, p. 577). The effect of culture on pain assessment is reviewed in Chapter 5.

The Role of the Pre-Meeting

A pre-meeting was the key to resolving the dilemma of how to proceed with the care of John Madison, a patient I had cared for over several months before his admission to the ICU. A pre-meeting helped the care team come to a consensus and decide how to communicate their concerns to Mr. Madison's wife, Alana.

John Madison was a 56-year-old man with refractory progressive pancreatic cancer. He had spent six weeks recuperating from a series of infectious complications related to his chemotherapy and was stable enough for discharge to a rehabilitation facility when he developed a pulmonary embolus and was intubated. His wife had brought him more than a thousand miles from their home in Barbados, hoping that he was eligible for an experimental treatment. He had made her promise, however, that she would not let him die in this strange city, that she would bring him home if he got worse.

We had met the Madisons weeks before the intubation, when we were asked to help with his pain management. We had spent many hours talking with Alana. During these talks, Alana described John as the love of her life, and the man who had rescued her from terrible social and financial circumstances (the details of which she declined to share).

The ICU attending physician, Dr. Bush, and the social worker, Nancy Lopez, asked us to participate in a family meeting that was being held because Alana was distraught. John could communicate with her by writing her notes, and he repeatedly begged her to take him home. Alana was asking everyone she could find to help her locate and pay for a medical flight so that John could die at home, as she had promised him. Our palliative care team asked Dr. Bush, Nancy, and John's nurses to have a short (15-minute) pre-meeting with us before we all met with Alana.

A pre-meeting ideally includes the attending physician, key consultants, and the social worker, nurses, and chaplain who know the family well. It should also include a representative of the outpatient team who has a long-term relationship with the patient and family. During this meeting, the group members review what they know about the patient's medical condition and likely prognosis, how much and how the family and patient want to be involved in making decisions, and what they know of his values and goals, either from direct communications with him or from his family. They also discuss what they know about his family's goals and values, especially those of his health proxy, and determine whether there are key differences between these values and the patient's. If there is no health proxy, they try to identify the best surrogate decision-maker for the patient.

Finally, at the pre-meeting the team members discuss their own agendas and how well or badly they match the priorities of the patient and his family. The group then determines what information is missing that the patient's family can supply. If the group members feel they know enough, they can come to a consensus on a plan of care to offer during the family meeting.

The "Third Story"

In our pre-meeting, though, it became clear that the ICU team members did *not* agree on what the meeting with Alana should accomplish, and it wasn't clear why. As the palliative care consultant, I realized that I might need to bring more to the group than just my expertise in symptom management or what Alana and John had shared with us prior to his ICU admission (just as you could offer more than just your oncology expertise or what you know from your relationship with the patient and family).

I thought I might need to use a strategy I learned from Stone and colleagues (2010), who advise that we "Move from certainty to curiosity . . . to understand the other person's story." To paraphrase: *What could they know or believe that will help you make sense of what they're saying?* I realized I needed to understand the "story" of each member of the medical team, and to share with them any differences I noted between their stories. If necessary, I was prepared to create for them what Stone and coauthors call the "Third Story." The Third Story accommodates all the "facts" in the first two stories and offers a different interpretation that allows for different conclusions. I find that in my role as palliative care consultant, the Third Story is often what breaks up the logjams; it releases the two sides from their dug-in positions and enables them to adopt a solution they can both agree on.

Understanding each of the ICU team members' stories was the first step. I asked what each of them thought was most important to Mr. Madison's care. It turned out that Nancy's priority was Alana and John's relationship and the work that needed to be done before he died. She wanted to focus on the futility of Alana's quest and on counseling her to use the time they had left discussing the things they needed to say to each other. Mr. Madison's nurses, however, wanted most of all for the team to respect John's wishes by supporting Alana's efforts to get them home. Dr. Bush surprised everyone. He revealed for the first time to all of us that what made him unwilling to even consider sending John home was what he saw as his professional duty to Mr. Madison. He felt he needed to find a hospital in Barbados that could deliver care comparable to the care John was receiving in our ICU, or John would have a terrible death. And he doubted there was such a facility in Barbados.

In this case, I did not need to create a "Third Story." Once they understood Dr. Bush's concerns, everyone agreed that they should be a main focus of the family

meeting. And Dr. Bush realized that he had found the words that would convey to Alana how seriously he took his obligation to John. We all decided that Nancy would first offer her thoughts to Alana, and then Dr. Bush would explain why he needed to transfer John to a comparable facility in his home country.

We were now ready to meet with Alana. Alana listened to Nancy's concerns, but told her that their "good time" had occurred when John was recuperating; what was happening now was a nightmare. Alana repeated her request that we help her take John home by financing the plane ride and contacting the appropriate home services.

It was only when Dr. Bush talked to Alana about their shared ideas of duty to Mr. Madison that Alana was finally able to understand our reluctance to send him home.

Alana, you have very eloquently explained to us the duty you owe John. You promised you would not let him die here, and you are doing everything you can to keep that promise. But I have a duty to him, too. I cannot send him somewhere that cannot give him the level of comfort we can give him here. If you can find a physician back home who agrees to accept him for care in a local ICU, and I satisfy myself that John can get the care he needs there, I would be happy to help him get a flight home.

For the first time since Mr. Madison was admitted to the ICU, Alana seemed to sense the team's compassion for her and her husband. She understood the concern that prompted Dr. Bush's resistance to the transfer and agreed that she wouldn't take John home unless it could be to an ICU. The pre-planning meeting, therefore, was crucial to our successful meeting with Alana. We aligned our goals and helped Dr. Bush find the words Alana needed to hear.

When You Have Never Met the Family

Although our palliative care team had known Alana and John Madison for some time before his admission to the ICU, we had never met Mr. Jordan's family. They did not even know that Mr. Jordan had cancer and had been undergoing chemotherapy treatments. Weissman (Weissman et al. 2010a, 2010b) provides tools for these discussions in two Fast Facts titled "Helping Surrogates Make Decisions," and "The Family Meeting: End-of-Life Goal Setting And Future Planning."

Mr. Jordan had just begun treatment for an aggressive large-cell lymphoma. He was the 70-year-old patriarch of a large family, with many children, grandchildren, and great-grandchildren. His oncologist told us that Mr. Jordan wouldn't let her

PRACTICE POINTS: ADVANCE CARE PLANNING WITH FAMILIES WHEN THE PATIENT CANNOT PARTICIPATE

- When you don't know the patient's wishes, consider consulting the palliative care team to help you hold a family meeting. When it is culturally appropriate, ask the family to help you determine what the patient would have wanted. Do not ask families, "What do you want me to do?"
- When you know the patient's wishes, share these with the family and ask the family whether the patient told them the same information. If all are in agreement, assure the family members that you will honor these wishes.
- If the family disagrees with what you know to be the stated wishes of the patient, consider consulting palliative care to work with the treatment team (including the chaplain, social worker, and nurses) and family to resolve the disagreement.
- If it cannot be resolved in this way, or if there is a disagreement among the treatment team members, obtain an ethics consultation.

speak with any of his family members. He said that he had not wanted his family to treat him any differently because of his illness, and he felt that this would inevitably occur if she spoke with his wife or anyone in his family. He had also not given clear answers to questions about resuscitation or being maintained by artificial means.

Now, he was intubated, suffering from neutropenic sepsis and pneumonia. His family members were the only ones who might be able to help the ICU team determine what he would have wanted, and our palliative care team was called to assist them. When I first met the Jordans, they were having an anguished family meeting with the chaplain, trying to decide what they should tell the doctors to do. After I introduced myself to the family, I explained that despite what the intern had asked them, they did not have to be the ones to make the decisions, that their ICU team was perfectly prepared and willing to make them, but we needed to know *"What* Mr. Jordan *would have wanted."*

By asking *what the patient would have wanted*, we maintain the ethical principles of Autonomy and Beneficence. *Autonomy* affirms that patients have an absolute right to refuse or accept any offered treatment. If we can discern their wishes, we will be acting as a *Surrogate* for them, expressing these wishes since they no longer can. *Beneficence* means that we should act in the best interest of the patient. We exercise beneficence when we use our knowledge of both the

long-term and short-term complications and the prognosis to advise the family what we expect the medical outcomes to be.

But families are the experts on the patients as persons: their goals, hopes, fears, and what functional outcomes would not be acceptable to them. Recommendations that physicians make with all that information in mind do not interfere with patient autonomy, they enhance it (Quill and Brody 1996; Epstein et al. 2010). For the interested reader, Nathan Cherny, MBBS, FRACP, FRCP, an internationally known oncologist and palliative care and ethics expert, has written his thoughts about how oncologists can profitably weigh the influence of the patient's culture with paternalism and autonomy in the difficult conversations they have with their patients. In the referenced article, Dr. Cherny discusses relational autonomy and introduces the concept of voluntary diminished autonomy as well as "soft" and "hard" paternalism (Cherny 2012).

Shared Decision-Making

Dr. Randall (Randy) Curtis, professor of medicine at the University of Washington School of Medicine and past president of the American Thoracic Society, is a palliative medicine expert and pulmonary intensivist whose research team has studied interactions between patient families and ICU teams in detail. They suggest that to help surrogates make the best decisions, and to minimize the burden that this responsibility places on them, our conversations with families in the ICU should not only provide medical information and elicit patient values and preferences, but also explore the family's preferred role in decision-making and deliberation (White et al. 2007).

Providing medical information and eliciting preferences. You can enhance this information sharing by setting up a private place for discussion; spending time *listening* rather than talking to the family; acknowledging and addressing their emotions; concentrating on what the patient's values and treatment preferences are; explaining what it means to be the "surrogate" decision-maker, checking for understanding, and supporting family decisions; reassuring them that you won't allow their loved one to suffer; and making sure that the communication is consistent, no matter which team member is delivering it.

Role in deliberation and decision-making. Families differ in how they want to participate in the deliberation and decision-making. For a family suddenly facing such a serious loss, who have never discussed these issues with the patient, the question of what *they* want done can be overwhelming. Some families want us to make all the decisions, some hope to drive the train themselves, but most fall somewhere in between (Shanawani et al. 2008). Family members who

serve in the role of surrogate decision-makers are under enormous stress, and a third of surrogates experience significant anxiety or other psychological problems from the emotional burden. The effects of playing this role usually last for months and may last much longer (Wendler and Rid 2011). Surrogates who played this role in the ICU setting "frequently used terms such as 'difficult', 'intense', 'painful', 'overwhelming', 'devastating', and 'traumatic'" (p. 342) and are at risk for developing post-traumatic stress disorder (PTSD).

For a moment, let down your guard and imagine yourself in the position of a family member being asked, "*Do you want us to take your mother off the ventilator?*" It's overwhelming, as though I just threw you a 30-pound medicine ball. You can also understand the answers that families give to house officers who ask such a question: "*I can't take the responsibility of turning off the machines*"; or "*We can't decide right now. We have to wait until [so-and-so] comes and we discuss it with [him].*"

You can enhance family satisfaction (White et al. 2007) and improve the bereavement outcomes of the family by ensuring that *concordance* exists between the family preferences for decision-making and how decisions are actually made (Gries et al. 2010). It became clear as we all worked with Mr. Jordan's family that they wanted the clinical team to make the decisions; it was too much responsibility for any one of them, or even for them collectively to let us know "*What Mr. Jordan would have wanted.*" And the team agreed to do that, thereby decreasing the chance that his family would later suffer from PTSD or depression.

"Ask-Tell-Ask"

When your patient is in the ICU, the ICU team may ask you, as the patient's oncologist, to lead the family meeting. The "Ask-Tell-Ask" approach will help you incorporate the elements of an effective family meeting that were listed above. You can use the VALUE mnemonic (Shanawani et al. 2008, p. 780) in these conversations to good effect:

V = Value statements made by family members
A = Acknowledge emotions.
L = Listen to family members.
U = Understand who the patient is as a person.
E = Elicit questions from family members.

You can also explore what roles they wish to have in the deliberations and the decisions.

Ask. After introductions of everyone present, address each family member in turn and *ask* how they think the patient is doing and what they think the likely outcome will be. Ask them what is of most concern to them, and what questions they have.

Tell. Only after you have heard from everyone should you begin to *tell,* to answer questions, correct misconceptions, and provide what you think are realistic goals of care. To begin the discussion about prolonging the patient's life using extraordinary measures, you might say:

Unfortunately, your [parent, child, spouse, partner, sibling, etc.] never told me directly what she wanted done if the only way she could be kept alive was by being connected to these machines. She never told me what to do if she died—whether the doctors should try to bring her back to life or whether she wanted to be left in peace. As her physician, carrying out her wishes is an important part of my responsibility to her, which I am happy to do. And I need your help to determine what she would have wanted.

If she were sitting here with us in this room, what do you think she would say? Did she ever let any of you know how she felt, possibly while you were all watching one of those medical TV programs like Grey's Anatomy*? Did she ever comment on relatives or friends who were resuscitated or needed machines to keep them alive? Sometimes people say things like, "I would never want to be kept alive if I had a disease that couldn't be made better," or "If I go, just let me be. At least I'd have my dignity, not like [so-and-so], who was on those machines for months before he finally died."*

Ask. At this point, you can *ask* again. This may feel like the right time to begin to explore how they want to be involved in the deliberations or decision-making. Ensure that you have answered all their questions, paraphrase what you heard them say, and ask for corrections or any additional material. And ask what you can do for them now.

You can offer a visit with a chaplain, or determine whether they simply want to be left alone to talk as a family. After the group breaks up, the social worker can stay with the family to help them with practical issues and continue the exploration of their preferences about shared decision-making.

Conflict

When withdrawal of life support is being considered, it is common to have conflicts between family members, between the family as a whole and the medical team, or between medical team members. One study cited in a paper by Shanawani and col-

PRACTICE POINTS FOR A FAMILY MEETING

- Hold a pre-meeting with all the patient's health care providers to establish consensus on "best choices" and identify family decision-makers. Ensure that key personnel can be present for the meeting, including someone who knows the current medical details and, ideally, someone from the outpatient team who has had a longitudinal relationship with the patient and family. Find a site and seats for all participants including the patient, if the patient wants to be present. During the meeting, let each person in the family who wishes to speak do so.
- ASK
  - —Ask the family to review with you how they think the patient is doing and what they see as the problems.
  - —Ask the family what they think is likely to happen.
  - —Ask the family what they hope for and what they fear will happen.
- TELL
  - —Explain the patient's current medical condition in global terms first, using lay language, and clarify the current prognosis; put any details of how each "system" is doing into the overall context of how the whole patient is doing.
  - —Answer questions about the medical condition, using lay language; check for understanding frequently.
- ASK
  - —Ask the family again, in light of this new information, what they hope and what they fear will happen.
  - —Delineate any key differences in priorities among the patient, health proxy, and medical care team.
  - —Explain to the family what is possible and what is likely.
- Work to achieve consensus.
- Document the personnel present, key information gained, results, and next steps in the electronic medical record as well as in the written chart.
- If the patient has asked not to be present, choose a group to inform the patient about the results of the meeting.

leagues (2008) found conflict between the family and the ICU staff or among members of the staff in almost 50 percent of the cases, and among members of the family 25 percent of the time. Moral distress can result from asking critical care nursing staff to continue aggressive care that the nurses feel is futile, making them feel that they are doing things "to" not "for" patients (Elpern et al. 2005).

Carefully run meetings among the staff or between the staff and family members can resolve these conflicts. Stone and colleagues (2010) suggest that we have three purposes in the meeting: "Learning their story; expressing your views and feelings; problem-solving together." They advise us again to move toward a learning conversation: "Arguing without understanding is never persuasive"; "People almost never change without first feeling understood"; "We have to understand the other person's story well enough to see how their conclusions make sense within it."

PRACTICE POINTS: LEARNING CONVERSATIONS

- You no longer have a message to deliver, but rather some information to share and some questions to ask.
- Arguing without understanding is never persuasive.
- People almost never change without first feeling understood.
- We have to understand the other person's story well enough to see how their conclusions make sense within it.

(Adapted from Stone et al. 2010)

Back and colleagues (Back, Arnold, et al. 2009) advise much as Stone and coauthors do (and in fact quote Stone et al., as you'll see below), that if we recognize the conflict, we first try to be curious: why is their answer to the same problem so different from ours? Stone would say "What else do I need to know for that to make more sense?" or "I wonder how I can understand the world in such a way that that would make sense?"

As Back, Arnold, and Tulsky write (p. 95): "Ask yourself: why is this otherwise well-meaning person wanting something different in this situation than what I want? The well-meaning attribution is important. To deal with this successfully, you cannot afford to frame the other person as an idiot because people will pick up, perhaps from your nonverbals, that you are dissing them. You will not be successful if the other person feels dismissed." Stone and coauthors offer: "It's always the right time to listen." Reframing may work, but if there's emotion, listen, question, and try to understand, not defend.

Here is the "Roadmap" that Back and colleagues offer for dealing with meetings when there's conflict (pp. 95–98):

1. Notice there is a disagreement . . . You may notice that you feel irritated, or "bored" ("This again?") or exasperated—your internal signals may be the most useful sensors for noticing conflict.

2. Find a nonjudgmental starting point . . . Why is this otherwise well-meaning person wanting something different in this situation than what I want?
3. Listen to and acknowledge the other person's story/concern/viewpoint . . . Douglas Stone describes three things to listen for: (1) their story about what has happened; (2) the emotions (theirs and yours) generated by what happened; and (3) their view of their identity—how does it shape their views. They add: "If the block to their listening is that they don't feel heard, then the way to remove that block is by helping them feel heard—by bending over backwards to listen to what they have to say, and perhaps most important, by demonstrating that you understand what they are saying and how they are feeling . . . unexpressed feelings can block the ability to listen."
4. Identify what the conflict is about, and try to articulate it as shared.
5. Brainstorm options that address the shared concern.
6. Look for options that recognize the interests of everyone involved.
7. Remember that not every conflict can be resolved.

Of course, sometimes a family tells the medical team that they don't care if the patient did not want life support, they want everything done anyway. In fact, that's not an uncommon reason for calling a palliative care consult. The family members may cite religious beliefs that mandate doing everything to stay alive, hopes for a miracle, or a belief that no matter what the patient told the health care team, they know what the patient really wanted. Some may be simply unable to imagine life without their loved one.

Engaging clergy, social workers, and other counselors can often provide support for these families; providing spiritual support, a forum for voicing religious beliefs and values, and having a proactive approach to medical decision-making may all be useful (Widera et al. 2011). These professionals can both support the family and help you unravel unspoken concerns so that you eventually reach a mutually agreeable plan. Ongoing attention to the patient's comfort, frequent check-ins with the family to see how they are doing, and exploration of new concerns as they arise help the family during their anticipatory grieving process and often lead to their ability to see that the hoped-for recovery is not going to take place. I discuss in Chapter 4 how to help the families who are hoping for a miracle.

Ethics Consultations

If conflict persists, then ask for an ethics consult (Fine 2010). Many hospitals have an ethics committee that develops guidelines (that are then approved by all clinical services) in such areas as advance care directives, withholding or withdrawing life-sustaining treatment, consent from patients with limited decision-making capacity, medical futility in care at the end of life, and disclosure of adverse events. Some hospitals also have individuals specially trained in medical ethics who are able to provide consultation services to help the dissenting parties come to a consensus about the path to take.

Dr. Albert Jonsen, a pioneer in the field of bioethics, and his coauthors offer a useful framework for using ethical principles to approach clinical problems (Jonsen et al. 2010). When approaching problematic cases, they suggest reviewing the (1) medical indications, (2) patient preferences, (3) quality of life, and (4) contextual features.

To obtain this information, both the medical caregivers (including all members of the medical team) and the patient and family are interviewed. An ethics consultant (who can be a physician, nurse, social worker, chaplain, or nonclinician specializing in medical ethics) initially interviews the hospital caregivers to clarify the medical history and hospital course of the patient, the facts of the situation in dispute, the values that are in conflict, the medical options that are available, and the reasons for the disagreement. If the dispute is between groups of caregivers (e.g., the nursing staff versus the doctors), the consultant will interview each group separately. If the conflict is between the caregivers and the patient or family, the consultant will interview all the caregivers together.

After the caregiver interviews, the ethics consultant interviews the patient and family, including the health care proxy, first to review the history leading up to the present conflict, and then to determine what they understand to be the facts, what they feel their options are, what they hope and fear will happen, what they feel would be the patient's wishes and values as they apply to this situation, and what they believe are the reasons for the disagreement with the caregivers.

After concluding these two meetings, the consultant facilitates a meeting between the two groups to try to resolve the conflict by reaching a consensus between the two. References at the end of this chapter provide more information about ethics consultations.

Summary

As this chapter illustrates, the early days after a diagnosis of a serious illness hold many challenges for patients and their clinicians. You must learn to recognize which conversations are likely to be difficult and why. You need to prepare yourself to tell patients bad news and then do so, clearly and compassionately, accepting whatever reaction ensues, be it despair, anger, or silence. There is no better way to demonstrate at the outset your commitment to being there to help. As you begin to understand why you might be reluctant to raise the subject of advance directives, resuscitation, and prognosis, you will be better able to initiate advance care planning and to discuss a prognosis that may be very limited. Knowing patients' priorities and goals, you can honor these when the patients are no longer able to communicate their choices by conducting effective meetings with their families using well-established techniques. When you don't know, you can employ shared decision-making and the "ask-tell-ask" methods to elucidate them. When goals differ, ethics consultation teams can help broker a solution.

Innovative programs that train oncology fellows in all these communication skills should create practitioners who are as well prepared to conduct these tough discussions as they are to give chemotherapy and treat its side effects. Such preparation, and the ability to grieve their losses, is likely to protect them from compassion fatigue, and to help them have long, productive careers.

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CHAPTER 2

Helping Patients Accept Opioid Pain Medication

Addressing Hidden Concerns
- Fear of Addiction
- Fear of Exhausting Effective Pain Medication
- Misconceptions about Side Effects
- Misconceptions about Religious Teachings

Other Techniques to Enhance Compliance
- Develop a Functional Goal
- Persuade Patients to Admit They Are Having Pain
- Unearth Hidden Agendas

Educating Colleagues

Summary

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Addressing Hidden Concerns

As physicians, one of our hardest tasks is convincing patients to accept our advice. This is especially difficult when we want them to take medications for a disease that is not bothering them—hypertension, for example. But I have found an equally strong reluctance on the part of many patients, even those in severe pain, to accept my prescriptions for opioids.

Studies have indicated that patients, families, and physicians share a number of fears and misconceptions about opioids that contribute to these drugs being underprescribed and infrequently used, whether for pain, dyspnea, or cough. In my experience, patients and their families rarely initiate discussions of such concerns when I recommend opioids. Their *unasked* questions can prevent them from accepting the relief that is available, however. I therefore assume that patients and families have all these fears and that I need to dispel the fears if I am to have any chance of getting cooperation with a prescribed medication regimen. These hidden concerns about opioids and ways to address them are discussed in the following paragraphs.

PATIENTS' AND CAREGIVERS' FEARS ABOUT OPIOIDS

- Fear of becoming addicted to opioids
- Fear of exhausting effective pain medication, leaving themselves with untreatable severe pain later in the course of their disease
- Misconceptions about health care providers' ability to prevent side effects
- Misunderstandings about religious teachings on the therapeutic use of opioid drugs

Fear of Addiction

Some physicians continue to resist prescribing opioids to their patients with cancer pain because they mistakenly believe that the risk of addiction is between 5 and 10 percent. Data indicate that the risk is far lower, however—fewer than 2 in 10,000 cancer patients with pain who do not have a previous history of aberrant substance use will develop addiction to an opioid drug.

Patients taking opioids for prolonged periods *will* become *physically dependent* on them: if the drug is abruptly stopped, they will experience a withdrawal syndrome. But addiction is not simply physical dependence; patients who are *addicted* want to use the drugs for their psychological effects—they *want to "get high."* They seek drugs for the escape they provide, and in their efforts "to get out of life," they continue to use drugs even when the drugs are harming them or others.

Patients with pain, on the other hand, simply want "to get back into" their lives. When the pain is gone, they no longer ask for pain-relieving medication. By prescribing opioids incorrectly, however, physicians can cause patients with pain to exhibit what looks like drug-seeking behavior, a condition called *opioid pseudo-addiction.* Someone with severe pain from breast cancer metastatic to bone may exhibit such behavior, for example, if prescribed oxycodone every 6 hours as needed for pain. The pain relief provided by oxycodone lasts 3 to 4 hours at most, leaving the patient with 2 hours of unrelieved pain. Such a patient might appear to be "addicted" because she asks the nurse for medication "2 hours early," but she is simply in severe pain because of inadequate blood levels of the opioid that provided pain relief.

Most patients, rather than developing drug-seeking behavior, strongly resist taking opioids because they share the physician's concern about the risks of addiction. The *Just Say No!* campaign of the 1980s, together with media portrayals of people who take drugs, remain powerful disincentives for patients considering the

use of opioids to relieve their pain. And if a son or daughter is or has been addicted to opioids, the patient may be reluctant to accept opioids even to control excruciating pain. These patients have expressed to me their fear that if they take the medication, they will experience the same disintegration they saw in their child.

PRACTICE POINTS: OVERCOMING FEAR OF ADDICTION

- Assume that the patient or family has concerns about opioids.
- Reassure them that the patient will not become a drug addict: cite studies showing that fewer than 2 in 10,000 cancer pain patients who take opioids become "addicts."
- Reassure the patient and family that if the source of the pain disappears, the patient will no longer wish to take the opioid.
- Tell them that addicts use drugs to get out of their lives; patients need opioids to get back into their lives.
- Draw analogies between the need for opioids and the need for other medications.

Earlier in my career, I was unaware of patients' reluctance to take opioids (and their families' uneasiness about administering them). I first became aware of this when I was faced with a patient whose pain seemed unaccountably resistant to therapy.

Opioids Don't Equal "Dope"

Mr. Pugh was a 68-year-old man with metastatic prostate cancer; his wife always accompanied him on his visits to my office. He was now bedridden by his pain. I had increased his opioid dosage several times, but the pain seemed undiminished. I was mystified until the visiting nurse called me from Mr. Pugh's home to report that none of the medication bottles had even been opened. When the nurse asked why, his wife replied, *"What makes the doctor think I would give him any of that dope?!"*

Neither the patient nor his wife, of course, had ever told me of their concerns about the opioids. In fact, as I noted earlier, I have never had a patient or a family member voluntarily disclose such fears when I first recommended opioid therapy. I suggest, therefore, that you proceed under the assumption that these concerns are present, even if not articulated. To break the ice, you might adopt an opening I have used successfully: *"Addicts use drugs to get out of their lives. You*

will be using them to get back into yours." For other patients, I might say, "*If you take this medicine, you know, you won't start stealing TV sets.*"

That usually gets a laugh and, along with it, an admission of a worry that is not entirely a joke. What can follow is a valuable opportunity for a frank discussion of the source and nature of the fears of this particular family. They are usually surprised that you have "guessed" their state of mind, and your ability to understand them so well may help them listen more closely to what else you have to say. It's important to explain that the patient won't "turn into an addict"—won't begin taking drugs for fun. Citing the findings I mentioned above (that fewer than 2 in 10,000 cancer pain patients taking opioids become addicts) will often provide additional reassurance.

Many perfectly reasonable people will have trouble understanding that taking a drug that causes physical dependence does not mean that they are "addicted" to it. Addiction carries with it dramatic negative connotations (stealing that TV set!), and it is particularly important that patients taking opioids not be locked into that word *addiction*. They need not label themselves as addicts.

To help patients understand the distinction, I use as an example someone in their family who may be receiving digoxin or insulin and draw attention to the similarities by saying,

Your aunt takes insulin every day for her diabetes. If she didn't, you know how sick she would get. These opioids are as important to your health as the insulin is to hers. Yes, your body is dependent on them, just as hers is on the insulin—in the sense that neither of you can stop the medicine suddenly or you'll get sick. But that doesn't mean you're an addict. You don't consider her "addicted" to insulin shots; you shouldn't consider yourself addicted because you need an opioid to relieve your pain.

I realize that the medications are not really comparable and that people are dependent on opioids and on insulin in different ways, but I find that this comparison helps demystify the drugs and makes it easier for patients to imagine themselves taking them.

It is easiest to get compliance when the patient is likely to need the opioid for only a short time. In such circumstances, you can reassure the patient that you'll taper him off the drugs as soon as he doesn't need them anymore. For example, to someone receiving radiation therapy to a bone metastasis, you might say, "*You are very likely to have less and less pain as the radiation treatment works. I'll follow your progress closely and decrease the medication as you find you need it less. If you don't need the opioids anymore, I'll stop them the way I do any other medication.*" It seems easier for patients to preserve their self-esteem if they consider that they are taking opioids to relieve the pain "just until the treatment has time to work."

Your assurance that you will wean them gradually and safely usually removes the last obstacle to their accepting your recommendation.

Fear of Exhausting Effective Pain Medication

Patients who resist taking opioids may be thinking, *"I can stand this pain now. But what if it becomes worse later?"* Their pain may be "only" moderate now, and they fear that if they take *any* opioid now, they will have "used up" the strongest medication available. Perhaps you, too, have had patients say, *"But if I take this now, what will be left if the pain gets worse?"* And family members' past experiences may have contributed to such concerns. The mother-in-law of one of my patients had died fifteen years before from cancer, with a course marked by uninterrupted pain. Having seen her mother's suffering, this patient's wife was understandably skeptical about my ability to provide comfort for her husband as the disease progressed.

You can reassure patients and their families that many pain-relieving medications are now available that you'll be able to give them later on (I discuss these in detail in later chapters). They can go ahead and take the recommended medicine now, knowing that if the pain becomes worse, there will always be a medication strong enough to relieve it.

Unfortunately, as you know, many patients may not be willing or able to articulate this concern to you. To anticipate and allay it for them, you might say something like: *"You cannot use up pain medicine; there's always plenty more where that came from. I've prescribed a low dose of the opioid for now, and I can always give you more of it, or we can change to a stronger medicine later if you need one."*

By thus encouraging patients to take opioids early in the course of their disease, you will be able to restore to them months or years of virtually normal, functional life. Their cancer burden is at its lowest, and because you have eliminated the pain, they will be able to work, perform most normal everyday tasks, and enjoy life. During this time they can be virtually pain-free and reassured that they have in no way diminished their chance for effective pain relief in the future.

Misconceptions about Side Effects

Patients may also resist taking opioids because of adverse side effects they have experienced in the past when taking a mild opioid, for example, after a tooth extraction. I remember well the experience of a colleague of mine with codeine. When she was ending her intern year, her L5–S1 disk herniated—she had fallen

on the ice that winter and, over the following months, had apparently lifted too many patients. At any rate, she was unable to stand and, as she was living alone at the time, was admitted to the hospital. After the first shot of morphine, which relieved her pain, she was given one or two shots of meperidine (Demerol).

But upon awakening the next morning in severe pain, she was offered only codeine. She found it so profoundly nauseating that she took it as infrequently as possible. What was worse, though, she said, was her realization, two weeks into her hospital course, that she hadn't had a bowel movement. She had never thought to ask for a laxative and one had never been offered. The discomfort of the eventual evacuation, exacerbated by her herniated disk, convinced her that opioids were something she'd *never* accept again.

And she is a physician. It is easy to understand why patients with similar experiences may refuse to consider opioids, even though they may be suffering from moderate to severe pain. Even the anticipation of uncontrolled constipation, nausea, or a "doped up" feeling is often unpleasant enough to prompt patients to refuse. We must let patients know that we are aware of these side effects and intend to prevent as many as we can, and that we will offer treatment for those we cannot prevent. (A full discussion of the prevention of constipation and the treatment of nausea and other opioid-induced side effects is given in Chapter 6.)

Constipation. I have found that the anticipation of constipation can be an especially serious problem in the elderly, for whom the daily bowel movement seems necessary to a sense of well-being. One of my patients, Mr. Salieri, had pain that was well controlled by 90 mg of oral sustained-release morphine twice a day. But because he could not alleviate the accompanying constipation using only "natural means" (prunes, fiber cereals), he refused to take anything stronger than ibuprofen, despite the intensity of his pain. Eventually, he agreed to take the morphine because his constipation was relieved using senna. He considered this an acceptable drug because he found it in a health food store.

Other side effects. You can also reassure patients about the other common side effects: feeling "doped up" or sedated or having nausea. The "doped up" feeling usually goes away after the first few days of therapy. The other side effects are usually relieved by switching to another opioid, since each opioid has a different side-effect profile. Opioid-induced nightmares and hallucinations, for example, may disappear if the opioid is changed. Urge your patients to let you or your nurse know if problems persist so that you can prescribe a different agent that will relieve the pain just as well without causing the troublesome side effect (see Chapter 6).

Misconceptions about Religious Teachings

Finally, patients and their families, and even health care professionals, may be leery about pain medicines because they have misinterpreted or are misinformed about what their religion teaches on the subjects of drugs, pain, suicide, and euthanasia. There are strictures in some religions, such as Roman Catholicism, against suicide, euthanasia, and the use of illicit drugs. Patients and their families may mistakenly think that these prohibitions apply to opioids prescribed for pain relief. They may believe that they cannot take (or give) doses of opioids that would relieve pain but might shorten life, because they would be committing suicide or assisting euthanasia.

The Church's position was stated first by Pius XII in 1957 and reiterated in the 1994 and 1997 editions of the Catechism (*Catechism of the Catholic Church* 1997, Subheading I, Euthanasia, verse 2279):

> Even if death is thought imminent, the ordinary care owed to a sick person cannot be legitimately interrupted. The use of painkillers to alleviate the sufferings of the dying, even at the risk of shortening their days, can be morally in conformity with human dignity if death is not willed as either an end or a means, but only foreseen and tolerated as inevitable. Palliative care is a special form of disinterested charity. As such, it should be encouraged.

This teaching is in contrast to the prohibition of the illicit use of drugs (*Catechism of the Catholic Church* 1997, Subheading II, Respect for the Dignity of Persons, verse 2291):

> The use *of drugs* inflicts very grave damage on human health and life. Their use, except on strictly therapeutic grounds, is a grave offense. Clandestine production of and trafficking in drugs are scandalous practices. They constitute direct co-operation in evil, since they encourage people to practices gravely contrary to the moral law.

Pain medication given or taken to relieve pain is morally acceptable to the Church, even if its use results in a shortening of life. This is the so-called doctrine of double effect. If the intent of giving the medication is to relieve pain, an unintended shortening of life is acceptable. In fact, there is very little if any credible evidence that pain medication given carefully and titrated to a patient's pain actually shortens life. The rare exception might be patients with far-advanced obstructive lung disease, in whom increasing hypercapnea might have that effect. But even in that situation, the stricture against "use of drugs" does not

apply. The physician or family member who gives medication to relieve suffering is not considered to have used drugs illicitly or to have participated in any form of euthanasia; the patient taking such medication is not considered to have committed suicide.

Physicians, nurses, and other health care providers may not be familiar with this teaching. One of the hospital nurses who cared for many of my patients attended an in-service class I was giving about pain, and when I discussed this subject, she burst into tears. She told me that for more than ten years she had been giving opioid medication to terminally ill patients to relieve their suffering but had assumed each time that she was committing a mortal sin. The relief she felt was palpable. And when I have pointed out the Church's teaching on this to many Catholic patients and their families, their relief was apparent as well.

Most Orthodox Jewish opinion, as well as that of Islamic leaders, also supports this doctrine of double effect. Pain medicine can be given even at the risk of shortening life. Intent is the key in all these cases. As one of the Islamic opinions clearly stated, "Intention is beyond the verification by the law," but according to Islam, "it cannot escape the ever watchful eye of God Who according to the Qur'an 'knows the treachery of the eyes, and all that hearts conceal' " (Qur'an 40:19). Some Muslims who need pain medication, however, will resist accepting even parenteral doses during the month of Ramadan. They may not be aware that the Qur'an relieves the sick of the burden of fasting during this month.

Eliminating these powerful misconceptions can allow Catholic, Jewish, and Muslim patients to attain the relief they need, along with the spiritual reassurance that what they and their families are doing is right. Observant Buddhists pose a more serious challenge. Their search for awareness may induce them to refuse pain medication if it interferes with the required meditation practices. Here, the suffering may affect the staff more than the patient, who accepts it as a necessary part of his spiritual life.

Other Techniques to Enhance Compliance

Even after you have dispelled the fears of patients and their families, answered their unasked questions, and corrected their misconceptions about opioids, you are likely to find some patients who continue to resist taking opioid medications. Many patients are discouraged from trying them because they assume the discomfort they suffer is part of their condition and cannot be improved. Others harbor hidden agendas that we must bring to light.

PRACTICE POINTS: ENHANCING COMPLIANCE

- Reassure patients that taking opioids now will not preclude their obtaining relief later, even if they develop more severe pain.
- Reassure patients that opioid-induced side effects can be managed with additional medications or by using a different opioid.
- Explain the doctrine of double effect and correct misconceptions about religious teachings on opioids.
- Help patients identify a meaningful functional goal that can be accomplished only if their pain is relieved.
- Enlist the help of family and friends to obtain a more correct assessment of patients who do not wish to distress you by admitting they are still in pain.
- Reassure patients that pain and disease severity are not related.
- Use careful questioning to uncover any guilt, denial, or anger.

Develop a Functional Goal

Unrelieved pain can be a major cause of disability for many cancer patients, but some patients incorrectly assume that their *cancer* has caused all the deterioration in their physical abilities. They feel that they have no choice but to accept their new limitations and learn to live with them, since they cannot even remember what life was like without the pain. They thus have no incentive to take pain medicine, because they think this would involve accepting side effects without gaining any meaningful benefits: *"What good is it to me to be bedridden and pain-free but doped up?"*

For many of these patients, however, the pain, not the cancer, is the problem. If they took opioids and their pain were relieved, they would no longer be bedridden and could function much more effectively in their families and communities. However, they have lost the ability to set goals for themselves outside some narrow limits. I suggest that you help such patients set functional goals. You might ask, "*What would you like to do that you can't now do because of the pain?*" Then, depending on the patient, suggest something like:

Would you like to make breakfast for your husband?
Would you like to take the kids to a ball game?
Would you like to go fishing?
Could you go to church and sit through the service?

Patients will often choose one of these or offer another reasonable goal. Using that goal, you can encourage them to take the pain medications by saying, "If

you take the medicines I've prescribed, you'll be able to do that—and other things you haven't been able to do for some time." I have found this to be a very successful technique to motivate patients who really would be able to function if they were out of pain. Even some people who have felt such despair at their helplessness and inactivity that they have expressed suicidal ideas have responded to these questions by setting realistic goals and, after taking appropriate pain medications, accomplishing them. Patients who had lost the support of their spiritual community were able to regain it and the comfort it provided.

Persuade Patients to Admit They Are Having Pain

Good patients. Some people simply want to be Good Patients. Despite their considerable pain, they appear brave, cheerful, and grateful during their visits with you and want to make you feel good when you see them. They are usually successful in this deception until you receive a call from the family, desperate because once again they have been up all night with the patient clearly in agony.

I believe that, on some level, these patients fear telling us that the medication we prescribed isn't working, because they are afraid we will become angry and reject them. I don't mean that they think we'll throw them out of the office, but they do feel we will be less glad to see them if they come with complaints instead of praise.

Even when the patient insists on continuing in the Good Patient role, the family can be of great help. I think you will find it useful to include them in your initial pain-management discussions with the patient. This lets family members know that you place a high priority on making the patient comfortable, and they are then more likely to tell you if the treatment regimen is not successful.

When I was still actively practicing oncology, I had several patients whose families called before the patient's scheduled appointment to let me know how things were really going at home. They always insisted I not tell the patient that they called, and during the patient's visit I usually found something that "led" me to the problem the family identified. Patients then often admitted that a family member urged them to mention the problem but said, "I didn't think it was worth bothering you about."

For some patients, opening this channel of communication to the family will be adequate. Others may be more comfortable working with a palliative care clinician. Consider referring patients to palliative care when you need help with a management plan, or when you think the patient would unburden himself more readily with a palliative care clinician. Patients and their family members may find in that relationship a much-needed additional source of support,

and you will have an expert collaborator. Patients may even live longer. Those with advanced inoperable non–small cell lung cancer who started seeing a palliative care specialist within three weeks of beginning their chemotherapy lived almost three months longer than patients in the same practice who saw a palliative care specialist only if they were referred by their oncologist (Temel et al. 2010).

Pain severity doesn't equal disease severity. Other patients are unable to admit how much pain they're actually experiencing because they fear that severe pain equals severe disease, and that the worse the pain, the sooner they are going to die. Such patients, understandably, will be afraid to admit to you how much pain they are having.

Just as you need to dispel patients' misconceptions about opioids, you may also need to anticipate this usually unstated misconception about pain. You can remind them that a small injury in the wrong place (such as a damaged tooth or a broken bone) can cause severe pain. This analogy may help them to understand that the severity of the pain is not related to the extent of their disease or to their prognosis. They may then be more willing to tell you honestly how much pain they are having.

Unearth Hidden Agendas

Finally, some patients seem inexplicably resistant to accepting pain medications. I have sometimes been successful in discovering their unexpressed agendas, among which I have most commonly found guilt, denial, and anger.

Guilt. Some patients, despite our best efforts, seem to resist all attempts to relieve their pain. I have been amazed at the range of reasons for this. One Vietnam War veteran finally admitted to me, "*I'd rather burn now than burn later.*" He never told me what it was he thought he needed to atone for, but he clearly felt that the suffering he was now experiencing would save him from an eternity of punishment after he died. A week or so after our discussion, he allowed me to prescribe medication; several weeks later, he died pain-free.

I was so grateful that I had been able to convince the patient to trust me enough to reveal his feelings. If I'd initially had more insight into his distress, I could have enlisted the aid of a psychologist or chaplain to help him uncover, share, and perhaps relieve his spiritual suffering much sooner.

Alan, a patient I later consulted on with far-advanced HIV-AIDS and meningeal spread of an AIDS-related lymphoma, was just as challenging. Despite all our efforts, he continued to complain of severe pain and paresthesias in both lower extremities. In the course of discussions with our social worker, Alan re-

vealed that he yearned to see his 8-year-old daughter, who was living with her mother, his former girlfriend. The social worker was able to locate his girlfriend and let her know that Alan was dying and that his last wish was to say good-bye to his daughter.

We never discovered what had gone on between them, but his girlfriend angrily refused. We were crestfallen and almost afraid to let him know that we had failed. But our social worker finally told him, with me in tow for support. To our surprise, Alan's face lit up with an almost beatific smile. He said, "Well, at least I tried," and fell asleep. When he awoke, he was a different man. The anguish was gone and, along with it, his complaints of intractable pain. And his death was a peaceful one.

Denial. Other patients seem to be using the pain to help them deny the extent of the disability caused by the cancer. The family of a woman who had widely metastatic breast cancer and had been bedridden for months was distraught at my seeming inability to decrease her pain. Whatever treatment we tried, the pain was always a "10" or "excruciating." When I finally asked the patient what she would do if she did not have the pain, she told me quite seriously that she would be skiing in Vermont. Her answer told me that her complaint of pain would never cease because, if it did, denial, her main defense mechanism, would disappear. She would then have to deal with what the *cancer*, not the pain, had done to her.

Once I understood this and explained it to her family, they were able to use other measures to assess the efficacy of the pain medicines (see Chapter 5). Functional measures (was she eating? sleeping? interacting with others?) revealed that the opioids were, on some level, working. Her family began to feel comfortable using these measures to adjust the drugs and became satisfied that they were providing all the comfort they could.

Anger. Some patients are angry at us, or at medicine, but either do not find it acceptable to tell us or have buried their feelings so deeply that they don't realize how hostile they are. They do know that they feel bad and want us to relieve their distress. They are likely, therefore, to continue to complain of "pain" until we are able to eliminate the source of the rage.

I find that asking "*What do you think is causing the pain?*" is a good way of detecting the anger in cancer patients who complain of pain but in whom I cannot find an anatomic source. Once the cause is elucidated, it can often be eliminated.

Anger Masked by a Complaint of Pain

Mrs. Lange reported persistent abdominal pain one month after a complete resection of what was found to be a localized recurrence of colon cancer at the

anastamotic site. To my surprise, in answer to my question on what she thought was causing the pain, she replied, *"I think that the pain is from cancer that Dr. Shore left in there and that you're all hiding it from me. When I had my first operation, the doctor told me he 'got it all.' Now I find out he lied to me. It came back, and I had to have another operation. Why should I believe you now when you tell me that there's no cancer left?"* A frank, open discussion about her anger toward, disappointment in, and distrust of all doctors followed. At future visits we continued our discussions, and the pain complaints ceased.

Discovering the source and letting her express her hostility was more effective in relieving her distress than any opioids I might have mistakenly offered.

For these patients suffering from guilt, denial, or anger, the pain served its purpose so well that, on some level, they did not want it to be relieved. Your efforts need to be directed at understanding their complicated agendas. Once you do, they may allow you to relieve much of their distress. Other sources of distress that patients report as pain are discussed in Chapter 5, where I discuss pain assessment.

Educating Colleagues

All these concerns about giving or taking opioids are shared not only by patients and families but also by physicians and the nursing and other staff encountered by patients in the hospital, the emergency room, or other physicians' offices. Even if you are comfortable with prescribing opioids and have explained their importance to your patients and their families, your best efforts can still be undone if any member of the health care team is not on board.

Physicians and nurse practitioners may still harbor misconceptions about their legal liability when they prescribe effective doses of opioids, even for patients with far-advanced disease. They may feel that the high doses these patients need will cause the prescriber to be investigated, prosecuted, and even disciplined. *Undertreatment* of a patient dying with cancer, however, is more likely to result in legal consequences. The U.S. Supreme Court recognized the right to maximal pain and symptom relief in *Vacco v. Quill*, which supported the use of whatever medication was needed to relieve suffering, even if there was a chance of hastening death. In 1999, Oregon's Board of Medical Examiners disciplined a physician who grossly undertreated the pain of six of his patients. In California, a suit brought by the family of a patient who was undertreated resulted in continuing medical education (CME) requirements in pain management and care at the end of life.

Staff nurses and interns, too, can unwittingly sabotage the pain-management plan and the patient's trust in the physician.

How Uninformed Staff Can Contribute to Patient Distress

One of my saddest memories is of a patient with extensive multiple myeloma who had been admitted for an unrelated condition, biliary obstruction due to gallstones. Mr. Hines had a previous history of alcohol abuse. One of his sons had been a heroin addict, and this had severely affected Mr. Hines's entire family. It had taken me a while, but I had finally convinced Mr. Hines that to achieve his goals, he needed the 90 mg of sustained-release morphine he was taking three times a day. Prior to his hospitalization for biliary obstruction, he had been active, pain-free, and free of any significant side effects from the medication.

But when I visited him after he was settled into his hospital bed, he was a very depressed and angry man. He greeted me with, *"I'm not going to take that morphine anymore, ever!"* I asked him, *"Why? What happened?"* He replied,

I told the intern what my usual medications were, and she said, "Isn't that an awful lot of morphine? I've never seen anyone who took that much morphine. Are you sure you really need it?" And then I heard her repeat the same thing to the nurses outside my door. They all looked in at me like I was the world's worst person. They think I'm an addict!

Are they right? You didn't seem to think the morphine dose I was taking was unusual, so it never occurred to me that it was a particularly high dose. But I don't want to go through what my son went through or shame my family. So I don't want any more of that morphine; I'd rather deal with the pain.

In one short conversation, the intern had unwittingly undone everything I had worked so hard to achieve with Mr. Hines. He felt terrible about himself and was angry at me for misleading and betraying him. Fortunately, he and I had a relationship of many years' standing. I was able to convince him that the dose he was taking was not at all unusual for someone with his condition, that I had many patients using much higher doses of opioids, and that if the intern had not yet taken care of anyone taking that dose of morphine, it was due to her lack of experience with cancer patients in pain, not to any problems in his character. I promised I would speak to the intern and the nursing staff, and he finally agreed to continue taking the morphine.

Despite the many advances in understanding and treating cancer pain, we still have a long way to go. We should not be surprised if some of our co-workers

still harbor fears and misconceptions about opioids and the patients who take them. Try to be attuned to comments that reveal these underlying feelings on the part of the physicians or other staff who care for your patients, and use such occurrences as opportunities to change their attitudes.

Years ago, I focused my efforts on the house staff and nurses who were caring for my hospitalized patients. I used the rather crude device of taping a note to the front of the patient's chart, which said, "*If you feel uncomfortable ordering or giving the opioid dose we recommend, please page me.*" This engendered a number of conversations and prompted several lectures and in-service classes on nursing units. In these sessions I tried to explore all the issues mentioned in this chapter and asked nursing staff to share their reservations with me so that we could work to resolve them.

Now, our palliative care team gives house staff, physician assistants, attending physicians, nurses, and nurse practitioners a pocket-sized "pink book" that includes a copy of Table 6.5, Commonly Used Opioids: Equianalgesic Doses (see Chapter 6), the "Faces scale" and other pain assessment tools, as well as information about non-opioid and opioid medications and opioid conversions. All the information is also available online in our hospital's intranet. In turn, the staff members become the teachers. And when new house staff who are uninformed about correct pain management come on service, the nurses, physician assistants, and knowledgeable house staff are in a position to educate them. The palliative care team remains available to back them up, but the well-informed staff members are now the vanguard of our pain-management efforts.

Summary

Even when we wish to relieve our patients' pain, their fears and misconceptions about opioids can prevent them from taking our advice. By addressing these issues when we first prescribe opioids, helping patients set functional goals, getting them to admit they are having pain, unearthing their hidden agendas, and educating our colleagues, we will have done our best to make it possible for patients and their families to accept the help we have to offer. By bringing other clinicians onto the pain-management team, we increase the efficacy of our pain-relief program.

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CHAPTER 3

Working with Patients' Families

with Arden O'Donnell, MPH, MSW, LICSW

Family Structure
- Identifying Key Family Members
- Using a Genogram to Map Relationships among Family Members
- Family Roles

Assessing Family Functioning
- The Family as a System
- What Is Normal?
- Using the Circumplex Model to Assess Family Functioning
- Communication as an Intervention
- The Role of Culture

Families That Require Additional Support
- Longstanding Conflicts
- Personality Disorders or Severe Mental Illnesses
- Addiction
- Domestic Violence

Summary

Bibliography

A cancer diagnosis transforms patients, but it also alters the lives of their families and friends. Our patients are members of much larger family systems that both influence our patients and are influenced by them. As people get sicker, the importance and influence of family systems increase, reaching an apex when patients can no longer make decisions for themselves (Clayton et al. 2005). Oncology teams naturally include care for the family as a unit, but broadening our focus to the issues presented by some families can feel more complex than treating the patient. We will always have the expertise of our social work and psychiatry colleagues to help us care for the most challenging families, but it is surprising how much we can do on our own if we understand the basics of how families function and the important roles we play during times of transition and terminal illness.

Drawing from the field of social work and research on family therapy, therefore, you will find in this chapter tools, case examples, and insights to help you

and your team navigate family dynamics and optimize communication with all families. We will discuss family assessment tools and present a model you can use to assess family dynamics and to increase the overall effectiveness of your interactions and meetings with family members. We provide a section describing the variety of ways families seem "difficult" for us to work with, and highlight the need for expert help when mental illness, addiction, or domestic violence are present in patients or families. The primary author of this chapter, Arden O'Donnell, MPH, MSW, LICSW, will also add her personal insights and recommendations throughout.

Family Structure

Identifying Key Family Members

In today's world, *family* can be defined in many ways. The best way to find out is to ask patients directly who the important people are. Knowing whom the patient considers "family," and which of these people should be involved in decision-making, is essential. Many times a social worker or nurse will be able to provide you with a good assessment of family structure, dynamics, and overall functioning. If this is not the case, you can collect a reasonable amount of information through a few questions and with careful observation.

As a social worker, as soon as I walk into a room, I begin to gather information about the family system. Who is in the room? Who is missing? Who holds power in this family? Is there tension in the room? Does this family speak to each other with respect? Are there significant pictures or cultural or religious objects in the room?

I do this because I learned the hard way the dangers of not asking these questions first. We have all been in situations when we have spent a significant amount of time and energy with a patient and then a key family player arrived or belief surfaced and we had to start all over again.

I also know that an important part of a patient's end-of-life work requires mending and honoring past relationships (personal and spiritual), and that estrangements, conflicts, and guilt can influence end-of-life decision-making. I remember working with Mrs. Simone, a 76-year-old woman with ovarian cancer, who was making decisions about the placement of a g-tube. When her husband and son were visiting, she presented as upbeat and positive, but as soon as they left, she was tearful and needy. After several days of observing this confusing behavior, I uncovered Mrs. Simone's family secret: she had another son, who was estranged and living in California. Although she could not tell her family,

Mrs. Simone longed to see or speak to her son one last time; she needed help to work through her feelings about the past estrangement, perhaps to forgive him or herself, in order to prepare for the end of her life.

PRACTICE POINTS: KEY AREAS TO EXPLORE ABOUT EACH FAMILY

- Who is in the family? Who are the key players and who needs to be involved in information sharing and decision-making?
- What are the significant relationships and dynamics in the family? What role does this patient play? What are the key family stories around illness and death?
- What is the family's basic level of functioning?
- What are the spiritual and cultural beliefs of the family and how do these influence decisions about treatment and goals of care?

Using a Genogram to Map Relationships among Family Members

Information about a family can be gathered in many ways, but one useful information-gathering technique is to construct a genogram. Although few clinicians take the time to draw out a genogram, an understanding of the concept and what questions one would ask to create one can give you a conceptual reference for how and how well the family works, what challenges it is facing, and what unfinished business it has. Answers to all of these questions will help you care for your patient as a part of that family.

Genograms are schematic diagrams by which you can represent family members and their relationships to one another, usually spanning three generations (Figure 3.1). Men are represented by squares and women by circles, with their age in the middle of the shape; the patient is indicated by a double circle or double square. You can also include dates of marriages and deaths. What makes the genogram dynamic and helpful, especially for family meetings when the patient's disease is far advanced, is that the diagram shows who is close to whom, who is cut off from whom and how long ago, and where there are areas of conflict. It can detail relevant family illnesses and deaths and the family members' previous experiences with these, where the family members are living now, and even the coping mechanisms of the patient and family (Rosen 1990).

Genograms can be helpful in working with families who seem to be stuck, as you'll see in Matt and Sally's case. Matt was a 62-year-old man with refractory lung

cancer. He had been admitted for pain control, and this had been achieved with the help of our palliative care team. The physician on our team asked me (Arden) to meet with this family because she thought they were very anxious and that Matt's wife, Sally, always seemed to have a reason to delay Matt's discharge. Even Matt's children, Jane and Jack, could not understand what the problem was; they thought he was ready for discharge home with hospice care.

To help me solve this riddle, I needed to know more about this family, so I created the genogram shown in Figure 3.1. To begin it, I drew the patient, 62-year-old Matt, as a double square near the center of the diagram. Matt had one sister, JS (one could add sibling family and details if there were significant connections or disconnections, but that was not the case here). He and Sally were married in 1974, and had three children. So I drew two vertical lines from Matt and Sally's icons, and connected them with a horizontal line with this date above it and then drew vertical lines dropping down from that horizontal line, to add Matt and Sally's children below them: 26-year-old Jane is the daughter (I drew a circle with her age in it), 28-year-old Jack is the middle son (same process, but with a square), and Matt Jr., is the elder son.

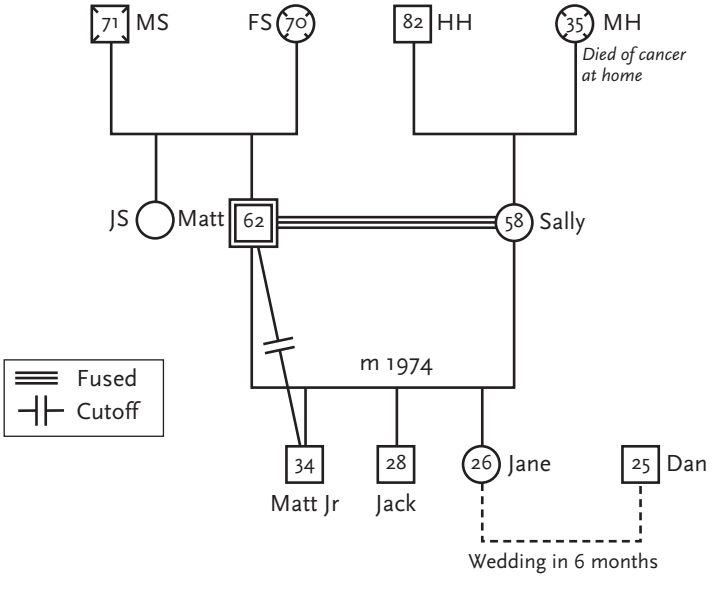

Figure 3.1. Genogram.

As I sketched out the genogram with Sally and Matt, the first thing it revealed was the existence of their older son, Matt Jr., whom they had not mentioned before. Matt became tearful speaking about Matt Jr., sharing that they'd had a falling

out two years ago, around the time of his diagnosis. When I learned that, I marked the line connecting Matt to Matt Jr. with slash marks to denote this ruptured relationship. I was able to provide education in the moment to Sally and Matt about the importance of our revisiting difficult situations that had occurred in the past and reinforced how healing this can be. Matt also shared that the upcoming marriage of his daughter (which I designated with a dotted line to her fiancé, Dan) was an important upcoming family event. Throughout the interview and in the nursing assessment, it was clear that Sally and Matt were very close, showing signs of *enmeshment*, discussed later in this chapter. To indicate that on the diagram, I added three parallel lines directly between their icons, to indicate an intensely close bond, a so-called fused relationship.

As the conversation progressed, Sally told me that her mother had died of cancer at 35, when Sally was only 16 years old, which gave me an opportunity to ask her directly about that experience for her. Sally tearfully told me that her mother had died at home, but, glancing at Matt in bed, she quickly brushed off her tears, saying, "I was very young when that happened." Her father was 82 and still living, though both of Matt's parents had died. I placed their initials next to squares or circles containing X's, which represent their deaths, and added their ages when they had died.

Armed with the information I now had, I simply needed to follow the clear roadmap they had given me during our conversation, a roadmap that highlighted where they needed help. First, I sought out Sally alone and revisited the death of her mother. She revealed tearfully the story of her mother's death at home, one that Sally felt was filled with suffering, along with Sally's own feelings of helplessness trying to care for her. Sally said that she has never even been able to reenter the room in which her mother had died. Sally was sure that if she took her husband home, he, too, would suffer, and she would be helpless to prevent that. While she was feeling guilty for not being able to take him home, she felt she could not tell him or their children the reasons. It is no wonder that she repeatedly "blocked discharge."

Next, I was able to revisit with Matt his relationship with his oldest son and help him and his family navigate the complexities of helping to repair this ruptured relationship. After this conversation, the nurse noticed a decrease in Matt's anxiety.

The genogram also helped the team with decision planning. When Sally and Jane asked whether a feeding tube would make Matt stronger, rather than discuss the benefits and burdens of a feeding tube in a vacuum, the team was able to ask them directly whether what they hoped for was that the feedings would help Matt be strong enough to attend Jane's upcoming wedding. They agreed that that was, in fact, the underlying question, since Matt had never expressed any hunger or

desire for the tube. We explained that it was unlikely that a feeding tube would achieve that goal and then supported the family during the difficult conversation that followed, which centered on ways to include Matt in the wedding even if he could not be there in person.

Later in the week, with Sally's permission, I helped her share with her family what she told me about her experience with her mother's dying at home. Both Matt and the children immediately understood, as did the medical team. Since Matt was not yet in his last weeks, Sally wanted to take him home and felt relieved that she had her family's support in making a plan that would include a transfer to an inpatient hospice facility for his last days.

The construction of a genogram is not needed in most situations, but I have found that with complex families or families like Matt and Sally who appear to be "stuck," it provides a graphic roadmap indicating places that would benefit from an intervention. I have also found that the graphic depiction uncovers family patterns and dynamics that don't come to light in a verbal family history.

PRACTICE POINTS: THINGS TO LISTEN FOR AS YOU COMPLETE A GENOGRAM

- Who is listed on the genogram but not present?
- Are there any major conflicts, cut-offs, or estrangements?
- Are there any strong bonds in the family?
- Are there any significant deaths? If so, how does the patient feel about them? How might these feelings affect views on the current case?

Family Roles

Roles are recurrent patterns of behavior by which individuals fulfill family functions and are an important part of healthy family functioning (Epstein et al. 1993). Understanding the roles of the patient and key family members can help you navigate family meetings and assist and support a family through decision-making processes (Mowery 2007). Here are the classic roles you are likely to find people playing. Look for them as you get to know your patients' families.

Patriarch or matriarch. Some families have one member who is the dominant decision-maker and is seen by everyone as the person in control. When the patriarch or matriarch is the patient, you can expect the family to struggle with decision-making. That was the case with Olive's family.

Olive was a 75-year-old woman who had run her family of five children for fifty years. Her attending physician called us in, saying, *"I've held three family meetings in the last two days, and each time, family members argued and contradicted each other. After all that, we still couldn't make any decisions."*

I held an informal family meeting and asked about what was happening. I learned that despite the fact that their mother was delirious, she was barking orders, and they were jumping to meet her needs and fighting over who was doing the most. I asked them, "*Can someone tell me what role your mom played in the family*" and they all shouted out *"Boss!" "Leader!" "President!"* The siblings said their father was passive and unable to make family decisions. It was clear that this was a pack that had lost its leader and that had yet to establish who would take over.

Once this was brought to light, the care team was able to support the family's transition into new family leadership. The team reinforced that Olive had named Maureen, her eldest daughter, as her health care proxy because she trusted to her to do what she, Olive, would have wanted. So if they allowed Maureen to represent them, they would be fulfilling Olive's wishes, as Maureen expressed them. In this way, I hoped that the family would accept the transition of leadership for the time they were in the hospital. The family discussed this among themselves and agreed that no one knew better than Maureen what Olive's wishes were, and that therefore she could speak for the family. The team's consistent reliance on Maureen during family meetings helped the family move the leadership role to her, and the family meetings became much less chaotic.

Peacekeeper and communicator. Some families have one person who serves as the central communicator. This individual helps ensure connections among all members of the family and manages conflict or difficult relationships when they arise. When this mediator is sick, families often struggle with how to talk to one another. I once met with a family in the ICU who was struggling with withdrawing the ventilator from their wife/mother. At one point, the woman's daughter said, "*We don't know what we will do without her; she is like the hub of our family. She keeps us all connected to each other. I wouldn't know what was going on with anyone if it was not for Mom!*"

After reflecting back to her that it sounded like she was afraid the family would stop communicating if her mother were gone, we discussed thinking about how communication could continue if the patient were not here. As the family began to volunteer ideas of how they could each take a piece of this role, they began to shift from fear of losing her to strategies of how they could keep her alive in spirit by honoring her commitment and keeping the family connected.

Teams who see that the family has lost a peacekeeper or communicator can help them by working to make it possible for all members of the family who should be present to attend family meetings. It is also helpful to have someone, often a social worker, talk with individual family members prior to meetings so that they can articulate their questions and feelings, feel prepared to ask their questions, and have all of them answered. The social worker can take this role temporarily and help the family members to assume pieces of the role.

Caretaker. The caretaker often takes responsibility for the emotional well-being of the family and may serve as a protector, working tirelessly to shield family members from unnecessary pain or discomfort. When the caretaker is the one who is sick, it is often difficult for her to accept help. Caretakers may also have a desire to die quickly to relieve the family of financial or caregiving burdens. One patient lamented, *"I can't get another procedure; it is too much for my husband. He can't take care of me—I have always taken care of him. Sometimes I feel like I should just stop all of this. I can't bear being a burden to my family."* You will need to encourage these patients to accept caregiving from family, and you will need to support and teach the newly identified family caregivers how best to care for the patient.

PRACTICE POINTS: QUESTIONS RELATED TO FAMILY ROLES

- Can you help me understand more about who your mother was in the family and to each of you? (Back et al. 2007)
- How is the patient affected by [his/her spouse/parent/child]'s role in the family?
- How will this family function without this patient?
- Whose role is missing from family meetings?

Assessing Family Functioning

The Family as a System

Although it is important to learn more about each family member and the role each plays in the family, clinicians also need some familiarity with how whole families work. Oncologists are not expected to be therapists, of course, but understanding the underlying principles of family systems therapy will enable you to identify a family's strengths and areas of difficulty, which can in turn help

you understand why patients make the choices they make. Although there are many branches of family therapy, the overarching premise behind all of them is that instead of focusing simply on individuals or qualities of family members, you focus on considering a family as a unit and on identifying patterns within a family (Nichols and Schwartz 2006).

What Is Normal?

In times of transition and crisis, even the most functional families can buckle. It is a rare family that doesn't benefit from some sort of additional support during times of extreme stress, but we all know that regardless of the level of stress, some families fare better than others. Can we predict which families will need the most support? Not always, but having an understanding of the basic level of family functioning can help us set realistic expectations for the time and effort each family will need.

Before we head into assessing family functioning, let's consider broadly the types of families we work with. Kissane and colleagues use the Family Environment Scale to measures a family's self-perception of their own cohesiveness, expressiveness, and capacity to deal with conflict (Kissane et al. 2006). Through this, they classified families into three broad classes (well-functioning, intermediate, and dysfunctional) to help identify which families are at high risk of having an especially tough bereavement. In one study that assessed the functioning of 257 families of palliative care patients, they categorized 29 percent as well-functioning families, 47 percent as intermediate functioning, and the remaining 24 percent as dysfunctional. We are likely to encounter a higher percentage of dysfunctional families, though, since the most dysfunctional families probably could not even participate in this study. Meyer and Block (2011) cite similar studies with the same range of difficult or dysfunctional patients.

Based on these data, we can predict that if we provide basic communication, leadership, and support, over one-quarter of our patients' families will be able to navigate end-of-life decisions and fare well with minimal additional support from our teams. These well-functioning families are not perfect, but we can assume that they show appropriate affect and attachment to each other (and to us), are capable problem solvers, likely agree with our treatment plans, and make the choices we might for our own loved ones. These are the families we consider resilient.

Just under half of our patients' families will have intermediate functioning. They will need some additional support to deal with the complexities of advanced illness, to understand and accept troubling medical information, to navigate the changing roles of family members, or to be successful in their struggles

with anticipatory grieving. With the support of regular communication and family meetings as well as short-term intensive support from social workers, psychiatrists, or psychologists around any particularly problematic issues, these families will be able to come together and support the patient.

The remaining quarter of our patients' families will be what Kissane terms dysfunctional. These struggling families create crisis even in the most reasonable situations. They "split" (pitting one family member against another, or the physicians against the nurses); they argue; they disagree. Overall they display irrational and irritating behavior throughout the course of the patient's illness. These families are viewed as unrealistic and at times hostile, and they may never develop a working alliance with the caregiving team. These are the families who take up the most of our time and leave us feeling exhausted or frustrated or questioning ourselves. These are the families with whom we need to set clear boundaries and expectations. And these are the families for whom we should call in reinforcements—palliative care teams, social workers, or other psychosocial clinicians.

My intent in bringing up this study is not to pathologize but rather to acknowledge that a significant percentage of our families need more help than one or two oncology clinicians can give. These families need a social worker or at times psychiatrist to help the family or the team serving them. Palliative care social workers have expertise in helping families navigate the stresses of end-of-life decisions in the midst of complex family dynamics or larger stressors, such as mental illness, addiction, or trauma histories. Just as you would call in a radiation oncologist when radiation therapy might be needed, when you realize a family might fall into the "dysfunctional" category, you should call in a social worker or, if none is available in your setting, another mental health professional. The next section will provide some tools to help you identify these families early in your relationship with them.

Using the Circumplex Model to Assess Family Functioning

We need to have a sense of the family's level of functioning because it can influence a patient's plan of care and even determine how we should interact with family members (Davies et al. 1995). The Circumplex Model can help. It is a systems-based theory that focuses on a family's level of (1) *cohesion*, (2) *flexibility*, and (3) *communication* and has served many clinicians as a guide to understanding overall family functioning (Olson and Gorall 2003). More than 700 studies have been published using this evidenced-based model and the associated Family Adaptability and Cohesion Evaluation Scale (FACES) self-report family assessment tool associated with it (Olson 2011).

We learned from these studies that families who score as "balanced" on the scales of cohesion and flexibility are higher functioning than those who are unbalanced (i.e., have very high or very low cohesion or flexibility). Once you learn how to place families in the right position on these scales of functioning, you'll know how best to use the meetings that you and your staff have with them to improve the family's ability to function and to care for the patient during this stressful time.

Level of family cohesion. Olson defines family cohesion as "the emotional bonding that family members have towards each other" (2000, p. 145). Key dimensions of family cohesion are the family's level of *emotional bonding*, how family members balance *togetherness* and *separateness*, standards of *acceptable family boundaries*, and *group decision-making capacity*. Families range from disengaged (very low cohesion), separated (low to medium cohesion), connected (medium to high cohesion), to enmeshed (very high cohesion). The families that work the best are those who are in the middle of the spectrum (i.e., "separated" or "connected").

Disengaged Families. The lack of family cohesion in *disengaged* families can create significant frustration for our teams as we try to talk with them. Members assume rigid roles, and individuals seem very separate rather than being attached or committed to each other (Nichols and Schwartz 2006). Members of disengaged families have a great deal of personal independence; they tend to grow even more distant to avoid conflict, and they are usually unable to turn to one another for problem solving or support (Olson and Gorall 2003). We see these family members sitting in separate areas of the waiting room and visiting at separate times, and we can be baffled at the lack of information sharing that seems to occur.

When working with one disengaged family, for example, the team had mistakenly assumed that Eileen, the patient's health care proxy, had asked her sisters to attend each of three scheduled family meetings. The team showed up each time, but no one else but Eileen was present. When I asked Eileen if she had called her sisters, I was shocked by her answer: *"I can't. I don't have their numbers."*

With disengaged families, therefore, you should not assume that information shared with one family member will be conveyed to another. You will need to be clear and provide consistent information about the patient's illness and make them understand that for the good of the patient, they have to find a way to come together, if only temporarily (King and Quill 2006; Davies et al. 1995). Your social worker can help provide a safe structure in which that can happen.

When they do come to together, these families need support, because they minimize interaction with each other to avoid conflict. They don't know how to communicate with each other in good times, and this is a crisis! Your staff or a palliative care social worker may need to help each individual feel safe contrib-

uting to the conversation, rather than struggle through disagreement after disagreement or long periods of silence.

Separated Families or Connected Families. Separated and *connected* families are the most "balanced" families, falling in the middle range of the cohesion scale, with good levels of attachment to each other and defined but flexible roles. Though they may disagree with each other, they are generally able to draw on a foundation of trust and caring during times of crisis. Often these families are drawn temporarily closer during an illness. They need some, but not extensive, support from you or your staff.

Enmeshed Families. Enmeshed families are also problematic. They have high levels of cohesion with an extreme amount of emotional closeness with each other. Enmeshed families have very diffuse boundaries and seem overly dependent and intrusively involved with each other. Loyalty to the family is demanded and independence strongly discouraged; many times these families have no clear leadership.

Suspect that you're dealing with an enmeshed family when all family members attend every appointment, when family members speak for each other, and when they use "we" when "I" is more appropriate. These families cannot tolerate disagreement, so they will at times prevent you from starting conversations, such as those about moving to comfort care, that could reveal different opinions. Enmeshed family members seem unable to envision life without any one of their family members, and this can greatly influence the end-of-life decisions both of the patient and the health care proxy.

When working with enmeshed families, social workers understand how difficult it is for one member to share concerns that she feels will not be welcome within the group, and so they will privately seek out the opinions of individuals. They may use the health care team as a model of a functioning group, each of whose members has a definite role, and help families define appropriate roles for each of them. Within the family meeting, we need to support everyone's right to speak up, saying something like, *"It is very normal that each of you will have some differing opinions about this, and I would like to hear from each of you."*

These families also tend to protect each other; not only will the patient tell you not to tell his family how sick he is, but his family will forbid you from telling the patient how sick he is!

One word of caution: don't mistake frequent checking in with each other, or presence of a large number of family members at the key family meeting with you, as being diagnostic of an enmeshed family. When assessing for level of cohesion, look for patterns of emotional closeness pre-crisis and be aware of the family's cultural norms. Many families will draw closer emotionally to each other during a crisis, and various cultures have differing levels of closeness. For

example, in general, white non-Hispanic Americans usually seem to have high levels of autonomy and independence, while Hispanic families may be much more connected, but they are not necessarily enmeshed.

PRACTICE POINTS: QUESTIONS THAT WILL LEAD TO INSIGHT ON FAMILY COHESION

- How close is your family? Are there people in the family the patient is closest to?
- How is information shared in your family? When and how did you find out about this illness?
- How does your family typically resolve conflict?

Level of family flexibility. The second guidepost in assessing family function in the Circumplex Model is family flexibility. Flexibility is defined as "how the family system can balance *stability* versus *change*" (emphasis mine; Olson and Gorall 2003). Key elements of this guidepost include family leadership, family negotiation style, relationship rules, and role relationships. Families range from *rigid* (those with very low flexibility), *structured* (low to medium flexibility), *flexible* (medium to high flexibility), to *chaotic* (very high flexibility). Here, too, the groups in the middle of the spectrum (*structured* and *flexible*) function the best.

Functional families have good levels of flexibility and are able to interchange roles based on personal strengths or necessity. For example, if the traditional caregiver of the family is not present, another family member can temporarily shift into that role. When a patient is dying, however, the family system must adjust to the loss of the patient in that caregiver role. Depending on the flexibility of the family and the role the patient held, there is often distress and there can at least temporarily be chaos as the system adjusts even in these healthy families.

Similarly, functional families can adapt to situations that are not stable, by being flexible and integrating the changes that need to occur. They trust that the new configuration they will achieve will be a beneficial one and will provide as much stability as their former configuration. There are likely to be more problems, however, in families with less or too much flexibility.

Rigid Families. Families with very low levels of flexibility (*rigid*) are ones that have strict and unchanging roles; one family member is in charge. Decision-makers are highly controlling; they make most of the decisions, and they are never questioned. These families have strict rules and boundaries about who does what and when, and who speaks and when.

If the family decision-maker is the patient, the family can become paralyzed. For these families, we should make strong recommendations or suggest they imagine that the patient is still making decisions, using questions like "If you father were sitting here now, what would he say?" If the family decision-maker is the health care proxy, you should not expect other family members to volunteer opinions or for there to be much family discussion; you may need to ask directly what each of the other individuals thinks, and this may not be received well by the decision-maker. You or the social worker should investigate whether there have been family estrangements and whether they are aware of how they have dealt with other family conflicts.

Many times you will discover family alliances or covert strategies they have used to balance their rigidity. This happened with Julia, a 68-year-old woman who was speaking with me before she had a high-risk procedure. I asked if she had ever thought about her advance care directives and whether there were any limits she would like on her care. *"Oh yes, I have those; in fact, I signed one of those living wills that says I don't want to live on machines. But I never told my husband about it!"*

She went on to explain his role as the decision-maker in their family and their disagreements about her views about code status. She could not stand up to him overtly, but she revealed that in a medical situation, her sister would come forth with the living will. After much work with her, she finally agreed to tell her wishes to her husband in a structured and supported family meeting and allowed us to put her living will in the medical chart.

Structured/Flexible Families. The most balanced families fall into the moderate level of flexibility, either being *structured,* which is characterized by democratic leadership and some sharing of roles, or *flexible,* characterized by a more egalitarian leadership and fluid sharing of roles when needed. These families are viewed as adaptable and able to make decisions, share leadership roles, and see others' points of view.

Chaotic Families. Chaotic families have excessively high levels of flexibility. They are characterized by unclear family roles, limited leadership, and erratic decision-making. These families appear impulsive, and decisions do not seem well thought out. They frustrate us greatly, agreeing to one treatment or home care option one day and completely changing their minds the next. Remember Olive, the matriarch of her family, whom we met in the Family Roles section above? She had a chaotic family. In addition to help in redefining roles, they benefited from high levels of structure and clear and consistent information and recommendations from us. Chaotic families benefit from pre-meetings with a social worker to help them sort through questions and thoughts before the team expects them to make decisions. At times these families will even need us to assign roles, such as "spokesperson" or "caretaker," to members.

PRACTICE POINTS: QUESTIONS THAT WILL LEAD TO INSIGHT ON FAMILY FLEXIBILITY

- How does your family usually make decisions?
- Do you generally get along? Does your family have a main caregiver? Decision-maker? (King and Quill 2006)
- How has your family dealt with other major transitions in life?

Level of family communication. The level of communication among family members is the third key marker in this model, both because of its role in assessment of family function and because this is where we can help families achieve greater levels of functioning. Good communication can support families as they try to establish or reestablish their balance and create a functioning system that can support the patient.

The level of communication in a family is a significant factor in its ability to adapt to the crisis of the patient's serious illness. Clinicians can measure communication levels by assessing the family as a whole. Families with good communication skills are able to listen to each other with empathy, express themselves clearly, respect other views, and share personal feelings about the situation. Good communication skills also include the ability to follow the conversation and problem solve without changing the subject.

For disengaged, enmeshed, rigid, and chaotic families, increased communication is usually the best and easiest intervention.

PRACTICE POINTS: QUESTIONS THAT WILL TELL YOU MORE ABOUT A FAMILY'S COMMUNICATION SKILLS

- How would you describe the level of communication in your family?
- How does the family usually make big decisions? (King and Quill 2006)
- Has your family ever been a part of making decisions for someone who was very sick? What was that like for the family?
- All families have disagreements, and with difficult decisions, this can feel even harder. How are disagreements usually handled in your family?
- What are your family's worries and fears?
- What is the hardest part of this for your family? (Back et al. 2007)
- What is most important to you now?

Communication as an Intervention

Using skillful communication, we can help families move toward the center, to a balanced place, on both the cohesion and the flexibility scales. Good communication not only improves a patient's adjustment to illness, adherence to medications, and pain and physical symptoms. It can also make a family meeting successful and greatly improve the family's satisfaction with care (Back et al. 2007).

Palliative care practitioners, social workers, clinical psychologists, and psychiatrists are skilled in communication, an integral part of which are listening, ability to regulate what we say even when we are feeling a strong emotion, and awareness of our internal reactions to others. When we are facilitating a family meeting, we will often share our internal emotional reactions, which helps family members understand that their internal emotional reactions are normal and often enhances communication among the family members present at the meeting. These families may simply have little experience in discussing difficult emotional issues; inviting family members to do this can shift family dynamics and create empathy for others in the family.

Remember Matt and Sally? Sally appeared to be blocking Matt's discharge home, and his children did not know why. But the social worker did and asked Sally's permission to share this with her family. Later, during a family meeting, the social worker, with Sally's prior consent, asked Sally directly about the death of her own mother and how she had felt as her mother had died at home. As she spoke, her adult children understood for the first time that their father dying at home would be very difficult for their mother and helped her make a plan to ensure that he would die in a hospice house where Sally was sure he'd get the best of care.

Most families, the ones Kissane would label as "well-functioning" or "ordinary," are able to adapt and cope with the stresses of terminal illness but simply don't have any experience with how to discuss the emotional or taboo subjects that arise when a loved one is dying. As we take the lead in these conversations, we help the family access its own strengths.

Questions that help families move toward a greater state of balance focus on increasing each member's ability to understand another's thoughts and feelings. Once these are understood, family members have a greater capacity to problem solve and support one another.

The Role of Culture

The last key component in assessing a family is to understand any cultural, religious, or spiritual beliefs that influence the patient and her family system. Culture is the behaviors and beliefs characteristic of a particular group, be it a social group, ethnic group, or even age group. With an increasingly diverse patient population, there has been greater attention to the understanding of spiritual and cultural beliefs, including those of patients with advanced illness (López 1997; Kagawa-Singer and Blackhall 2001).

Although each individual's perspectives are influenced by his personality, education level, and gender, cultural influences fundamentally shape patients' perceptions of illness, suffering, and death as well as the decisions they make during advanced illness (Kagawa-Singer and Blackhall 2001). Asking questions that reveal the family's story of the illness (their "narrative") and the influences of their culture on how they think the patient should be cared for can greatly enhance families' perceptions of being heard and understood. These influences range from the single-family level, apparent when someone says, *"Our family does not talk about feelings"* to the broader influences affecting those who come from cultures that have experienced longstanding inequities, societal oppression, or abuse.

At the end of this chapter, we provide reference articles and research highlighting cultural differences between specific populations. You can use these references to understand how to begin discussions with families about common cultural practices or concerns that you see in your patient population. An excellent online resource is the Stanford School of Medicine Ethno Med site (http://geriatrics.stanford.edu/ethnomed), which is organized by ethnic group and gives clinicians a quick overall view of each group, including their medical vulnerabilities, spiritual beliefs, and common cultural themes. The 2001 *JAMA* series entitled Perspectives on Care at the End of Life is also helpful. Several articles highlight different ethnic groups and use examples to describe the cultural influences and perspectives of that group as they affect the clinical decisions that patients and families are asked to make. The articles also include tools to assist us in being as helpful as possible.

Although certain beliefs may be more common in individuals with particular cultural backgrounds, making assumptions about a specific patient based on his culture can be not only unhelpful but damaging. In general, asking good questions and presenting a sincere curiosity about the spiritual and cultural beliefs of each patient or family is best.

Key areas that have been strongly linked to culture include views on sharing and communicating difficult information; the locus of decision-making; and the

role of the physician (Searight and Gafford 2005). African Americans, for example, generally want to be informed about the diagnosis and prognosis of their illness but are less likely than Caucasian Americans to feel included in the decision-making (Kagawa-Singer and Blackhall 2001). Patients from other cultures, however, may have significantly different views in these areas from those generally found in those born in the United States.

Although informed consent and truth-telling about the diagnosis is a major tenet of the U.S. health care system, many other cultures find it appropriate to withhold from patients the knowledge that they have serious medical conditions. In many parts of Asia, Eastern Europe, Central and South America, and the Middle East, withholding information is felt to be more humane (Gysels et al. 2012; Kagawa-Singer and Blackhall 2001; Searight and Gafford 2005). Physicians in these cultures might avoid speaking of the potential terminal condition by using terminology that obscures the diagnosis, speaking of the "mass" or "growth" rather than talking about the "cancer" (Kagawa-Singer and Blackhall 2001). Although this may not be something you are comfortable doing, having an understanding of the cultural norms and expectations of families can allow for a discussion about informed consent and can allow patient autonomy to be preserved while respecting cultural norms.

Who should make medical decisions can also greatly vary from culture to culture. Although the U.S. medical system places emphasis on patient autonomy and self-determination, many ethnic communities hold the values of collectivism. In a collective decision process, family members expect to receive medical information and make decisions without the patient's input. Asian, Mexican, and Mexican American patients may be more likely to want family members included as they make decisions or to delegate the decision-making to them (Searight 2005). In Asian cultures, filial piety, the expectation that children will care for their parents as a form of honoring them, can greatly influence decision-making. If, for example, you are speaking with an Asian family about hospice, be sure to emphasize the major role the family will continue to play as caregivers, because they will likely reject hospice services if they feel that another person will be caring for their parents (Kagawa-Singer and Blackhall 2001).

The degree of authority, respect, and deference given to physicians can also be tightly linked to culture. A family who had come from China to seek treatment for their son seemed to listen and understand when the team told them that we had no new treatments to offer him. But later, the team was dismayed to discover that the family was seeking care at another institution. Our misunderstanding may have come from not recognizing that, in their deference to authority, his family did not feel comfortable verbalizing doubts in front of the

doctors; that would have been disrespectful. Other families with similar beliefs may find it easier to just not follow our treatment instructions; without having visiting nurses or other eyes and ears in the patient's home, we might not understand why our intervention hasn't been helpful.

Although it is impossible to have a thorough knowledge of the many cultures of your patients, genuine interest in a family's cultural, spiritual, and religious beliefs is likely to enable you to provide culturally sensitive care with an understanding of the patient's health care preferences. You are also more likely to find common ground between your beliefs and those of your patients and their families.

PRACTICE POINTS: QUESTIONS TO GAIN CULTURAL COMPETENCY

- Is there anything that would be helpful for our team to know about your family, or your religious or cultural views on serious illness or treatment?
- Some people want to know everything about their medical condition; others do not. What is your preference?
- Do you prefer to make decisions about future medical decisions for yourself or would you prefer others make them for you?

(From Searight and Gafford 2005)

Families That Require Additional Support

We hope that we have introduced you to basic tools that you can use to assess, characterize, and navigate family dynamics. But there are situations in which you should always get help. Families with longstanding histories of conflict among their members; families that have a member suffering from a personality disorder, severe mental illness, or addiction; or families in which there is domestic violence usually have extreme imbalances in flexibility and cohesion, and their patterns of communication are rooted in dysfunction. These families will need referrals to psychiatry, social work, chaplaincy, addiction specialists, or domestic violence specialists. It is also important for you to set realistic expectations and to understand that you will be working in crisis-control mode with them.

Longstanding Conflicts

Dysfunctional families display a high level of conflict in and between members, and there is often a longstanding history of conflict within the family (Kissane

2006). It is key, therefore, to identify families in which one of the members was disowned, there is no contact with children, or some members are isolated from other family members. Have a social worker with you as often as you can when you meet with these families. If there is clear conflict in the room, the social worker will acknowledge it directly and set clear boundaries with a statement such as, *"I can see that you all have disagreements on a number of issues, but I am wondering if we can put those aside so we can focus on what is going on with your father?"* (Back et al. 2007). In many cases, however, the social worker will need to set up a more concrete plan to contain the disagreements. The King and Quill (2006) article "Working with Families in Palliative Care: One Size Does Not Fit All" gives concrete and important suggestions for dealing with conflictual families.

PRACTICE POINTS: STRATEGIES TO USE WITH CONFLICTUAL FAMILIES

- Set modest expectations about what level of collaborative decision-making is possible.
- Choose one clinician to lead and set ground rules for communication.
- Encourage family members to speak to you directly about issues rather than directing accusations at members.
- Remain neutral.
- Increase communication between providers to avoid mixed messages.

(From King and Quill 2006)

Personality Disorders or Severe Mental Illnesses

Families who have members with personality disorders or other mental illness are likely to fall into Kissane's "dysfunctional" groupings, and to be considered "difficult" (Meyer and Block 2011). These difficult patients likely function at chaotic levels of flexibility and with little cohesion. Unfortunately, we are rarely told that history either by the medical record or by a family member, but if we pay attention to the emotions patients evoke in us, we can identify the problem and get help.

If you find yourself feeling anger, guilt, or frustration when you're working with a patient, you have difficulty forming alliances with her, she doesn't come to appointments on time or adhere to your recommendations, or she's calling your staff repeatedly throughout the week (or throughout a day!), you are likely

dealing with one of these unfortunate patients (Meyer and Block 2011). We cannot address this topic fully here, but we suggest you read the Meyer and Block article "Personality Disorders in the Oncology Setting." If you're like us, you'll have many "Aha!" moments.

Even if you're not able to "contain" difficult behaviors, you'll be better able to identify these patients, understand their otherwise puzzling behavior, and work quickly to find a clinician who is expert in this area (or refer the patient to another physician who has access to such help). Specialists will advise you to be vigilant about giving clear and consistent information about the illness or any care options, because any mixed or conflicting messages the patient hears from you or your staff will cause the patient to "split" the members of your staff ("But she told me X when you told me Y") and fuel distrust. One patient like this is enough to disrupt an entire practice if not contained.

TOOLS FOR WORKING WITH PATIENTS WITH PERSONALITY DISORDERS

- Focus on building and maintaining a therapeutic alliance.
- Acknowledge and empathize with the real stresses in the patient's situation.
- Set consistent, appropriate expectations, limits, and boundaries.
- Evaluate patients for suicidality and homicidality.
- Hold ongoing personal and team meetings reflecting on the effect this patient is having on the team.
- Refer to another physician if you are not able to identify a psychiatrist or social worker who can work with your staff as they care for these patients.

(From Meyer and Block 2011)

Addiction

It is crucial to know whether a family's history includes alcohol or substance abuse. This information will provide important insight into family dynamics and the roles of family members. Two well-established screening tools are the AUDIT-C (Bush et al, 1998) (Figure 3.2) and the Opioid Risk Tool (Webster and Webster 2005) (Figure 3.3). They reveal this part of the family history and estimate the risk of aberrant use of alcohol or opioids by the patient.

1. How often do you have a drink containing alcohol?
Never (0) Monthly or less (1) Two to four times a month (2) Two to three times per week (3) Four or more times a week (4) _____

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
1 or 2 (0) 3 or 4 (1) 5 or 6 (2) 7 to 9 (3) 10 or more (4) _____

3. How often do you have six or more drinks on one occasion?
Never (0) Less than Monthly (1) Monthly (2) Two to three times per week (3) Four or more times a week (4) _____

TOTAL SCORE _____

Maximum score is 12. A score of 4 or greater identifies 86% of men who report drinking above recommended levels or meets criteria for alcohol use disorders. A score of >2 identifies 84% of women who report hazardous drinking or alcohol use disorders.

Figure 3.2. AUDIT-C screening tool.

Roles in families dealing with alcoholism. When one member has a substance use problem, the family dynamics shift. Family members are more likely to display anger, resentment, and guilt, and some may take on the roles of enabling or protecting the person with the problem. Several common family roles have been described for children growing up in alcoholic households, including the *hero*, the *comic*, the *lost child*, and the *scapegoat*.

The Hero. Most commonly, the *hero* is the oldest child. She is seen as the responsible child and was usually the one who excelled academically or socially despite the family dysfunction. She assumed the parental role many times when the parent was not present. Often she is named and respected as the health care proxy. When you recognize a "hero" in such a family, it can be helpful in discussions of care goals to ask, respectfully, that the other siblings be allowed to offer their opinions. It may be the only way they feel able to express a contrary view. I once asked a woman what she thought about the decision not to turn off her mother's ICD and she said, referring to the hero in their family, "*I don't agree but my sister gets to decide, just like she always has.*"

The Comic. The *comic* often plays a helpful role. This is the person who keeps things light and can serve to ease family tension during a conflict or provide an outlet for emotional pain. Most of the time, the comics are great to have in a family

	Enter score in box	*Score (Female)*	*Score (Male)*
1. Family History of Substance Abuse			
Alcohol	❑	1	3
Illegal Drugs	❑	2	3
Prescription Drugs	❑	4	4
2. Personal History of Substance Abuse			
Alcohol	❑	3	3
Illegal Drugs	❑	4	4
Prescription Drugs	❑	5	5
3. Age (Enter score if 16–45)	❑	1	1
4. Psychological disease			
Attention-deficit/hyperactivity disorder, obsessive compulsive disorder, bipolar disorder, schizophrenia	❑	2	2
Depression	❑	1	1

Total Score Risk Category **TOTAL** _____

Low Risk 0–3, Moderate Risk 4–7, High Risk >8

Figure 3.3. Opioid Risk screening tool.

meeting because they can bring in humor to lighten the mood, which can also open space for further conversations.

The Lost Child. A *lost child* is a sibling who may have been "lost" to substance abuse or mental illness, but they are still loved. Though they hold little authority within the family, they are people the family feel they need to protect. In one family, our failure to recognize the lost child led to repeated bouts of family chaos. She spent the night with her father every night, and we thought she was the person the family looked to for updates from us. So each morning the team would come in and give her the updates. After two mornings of post-rounds family chaos, we realized that this sweet daughter had a history of an anxiety disorder and would call the family after the team came in and give them anxiety-driven misinformation. The family, of course, would rush to the hospital and demand a team meeting. Things calmed down when we realized that and began to round on the patient only after other family members had arrived.

The Scapegoat. The *scapegoat* is the individual who is blamed for the family's problems. The family uses this strategy to deflect attention from the real problem, which is usually alcoholism in the house. In times of medical distress, you may find that this individual has again fallen into the role of being blamed when the family is unable to focus on the distressing issue at hand. You are likely to need the help of a social worker if you find that you're making no progress in discussing next steps, or goals of care, because of their inability to see what the real problem is.

Domestic Violence

Across their lifetime, one in every four women is a victim of domestic violence, and a much larger percentage of women are in relationships that involve extreme imbalances of power. Men can also be victims, as can the elderly. These imbalances affect family dynamics and an individual's decision-making. We should therefore be alert to any hints of a history of domestic violence or other emotionally controlling behavior when we are asking patients and families to make decisions about discharge placements or location of care at the end of life (Fisher 2003).

If you suspect or know there was domestic violence, if one member of the family or the partner seems to exert extreme power over the patient, or if there seems to be a lot of conflict or personal violence in a relationship, these are immediate red flags to involve a social worker or mental health professional. In situations when the batterer is ill, the victim may be unable to take on the role of decision-maker. When the batterer is the caregiver, it is essential that the team set clear boundaries around decision-making and consider including a domestic violence specialist and or an ethics consultant.

A complex ICU case may be illustrative of this dangerous and painful dynamic. The palliative care team was called to help with symptom management of a 65-year-old woman with multiple nonhealing postoperative wounds. Her husband exhibited extremely controlling behaviors that escalated as his wife got sicker. Nurses were afraid to work with him, and many clinicians felt that the team was being bullied into providing medical interventions based on his coercion and legal threats. He repeatedly accused the team of trying to "kill his wife."

Whenever she was alone with the ICU team, the patient would beg the doctors and the nurses to make her "do not resuscitate or intubate" (DNR/I) and allow her to die, but when her husband was in the room, she agreed with him when

he yelled, "You want to live, don't you? You must, and you do!" At one point the patient changed her HCP to her daughter and asked her to allow her to die, but after two days, her daughter revoked the proxy but would not talk openly about the reason. In this complicated case, it was necessary to involve specialists in domestic violence, psychiatry, and ethics to help the team navigate the complexities of the family dynamic. In the end, the medical team acted on behalf of the wife and set boundaries that the husband could not be in the room alone with her. She was made DNR and died peacefully there.

PRACTICE POINTS: SIGNS THAT YOU NEED TO GET HELP FROM PSYCHIATRY OR SOCIAL WORK

- Patient or family has a history of conflict or violence.
- Signs of a major mental illness or personality disorder in the patient or health care proxy.
- History of addiction.
- History or suspicion of domestic violence, elder abuse, or extreme power discrepancies.

Summary

We hope that the tools we describe in this chapter will help you identify the patient's role in the family, the general level of family functioning, and the areas of family dysfunction. Understanding the three fundamental dimensions of a family—*cohesion*, *flexibility*, and *communication ability*—enables you to set realistic objectives for what you can achieve with them as well as helping you begin to think how best to approach different types of families. Families that are balanced usually have the resources and skills to adapt the family system in a way that can deal with stress or a crisis; unbalanced families lack these resources and will need more time, assistance, and resources. To be most effective with them, you and your team will need to increase your level of communication, structure, and consistency in proportion to the level of instability in the family system.

Understanding the cultural beliefs of your patients is also essential to helping them and their families smoothly navigate decisions regarding therapy and those that arise at the end of life. A patient's culture is a foundational piece of who they are and influences how they view illness and death.

With families that have longstanding histories of conflict, past or present domestic violence, mental illness or addiction, you should call in a specialist.

Always be realistic in your goals and remember, it is not your job to change these patterns. Try your best to work within them to achieve the best quality of life for your patients.

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CHAPTER 4

Approaching the End

Components of a "Good Death"
Dealing with the Conflicting Views of Physician, Patient, Family, and Friends
- The Spectrum of Responses to a Terminal Cancer Diagnosis
- The Effects of Distance in Space and Time
- Isolation: An Unintended Consequence of Protection

Avoiding Patient Abandonment
Prioritized Symptom Lists
- The Patient's List
- The Family's List
- The Physician's List

Moving Forward to "Comfort Care"
- Making the Transition
- Impact of Religious Views
- Readdressing Resuscitation
- Anticipating Family Concerns
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Physician-Assisted Death
- Requests
- The Debates about Legalizing Physician-Assisted Death and Euthanasia

Self-Care
- Compassion Fatigue
- Grief Rounds

Summary
Bibliography

Components of a "Good Death"

We cannot change the downhill course of some patients with far-advanced illnesses. We can, however, strive to provide all patients with care and comfort as they die. Marilyn Webb, in the conclusion to her book *The Good Death: The New American Search to Reshape the End of Life,* lists ten components that she found to be present when someone died a "good death":

- Open, ongoing communication
- Preservation of the patient's decision-making power
- Sophisticated symptom control
- Limits on excessive treatment
- A focus on preserving the patient's quality of life
- Emotional support
- Financial support
- Family support
- Spiritual support
- The medical staff's not abandoning the patient even when curative treatment is no longer required

I too have found that, as in the initial days when the patient was adjusting to the diagnosis of cancer, communication is often at the heart of good patient care as death approaches. Providing family support, helping patients and families avoid fears of abandonment, and limiting unnecessary treatments are also crucial. In Chapter 10, The Last Days . . . and the Bereaved, I review how to provide sophisticated symptom control, as well as the other aspects of the clinical management of patients in their last weeks of life, and how to support their families both before and following the patient's death.

Although Webb's components of a good death are among the issues I discuss early in this chapter, I begin with communication because many of the problems that occur in the terminal phases of illness are due to problems in communication—between you and the patient, between you and the family, and between the patient and her family and friends. Some of these difficulties may arise because each of us (physician, patient, family member, friend) has a different view of the stage of the patient's illness and the remaining options for care. Others are unintended consequences of family members' efforts to protect one another from depressing information. Sometimes problems occur because the true source of distress is not clearly communicated. At other times, we physicians are to blame, because the words we use convey the opposite of what we feel or what we are trying to say, especially when we at-

tempt to explain why comfort-focused care is the only remaining reasonable option. I discuss each of these communication problems in the pages that follow.

I also review in this chapter what for me has been a very distressing matter—a patient's request that I help him kill himself or, worse, that I end his life. I examine why patients ask this of us and suggest how we can respond—whether or not we accede to their wishes.

Dealing with the Conflicting Views of Physician, Patient, Family, and Friends

Consequences of Emotional Asynchrony

My uncle John visited his neurologist because he was having difficulty speaking and new right-sided weakness, and he was found to have numerous brain metastases. Despite an extensive search, no primary cancer was found. He received palliative cranial irradiation, which led to some improvement.

His doctors asked me to coordinate communication between them and our family. I explained to our family that Uncle John was getting appropriate care but that his chances for prolonged survival, or even survival beyond six months, were small. His general internist, medical oncologist, radiation oncologist, neurologist, and I all agreed that there was no indication for further antineoplastic treatments, that symptom management should be our goal, and that his internist was in the best position to manage this. My husband and I, visiting my uncle, had found him to be comfortable but mildly confused, and exhausted by minor exertions such as going out to eat.

John's main source of distress, however, was the feeling that he ought to be doing something to fight the cancer—that was his interpretation of the advice he had been getting from friends and other members of the family. Some had suggested he go immediately to a nearby university-affiliated cancer center and sign up for experimental therapy. Others insisted that the NIH in Bethesda, Maryland, was the only place to be. Still others sent Uncle John alternative-medicine pamphlets and catalogs, extolling "natural products" and diet regimens they were sure would be effective.

Uncle John expressed to me his dismay at all this: *"I am so confused. I trust my doctors, and they tell me that there is no treatment that will make me live longer or better. But our family and my friends keep telling me that I should be doing something, and each one has a different idea of exactly what that should be. What do* you *think I should be doing?"* Although I explained to him many times that they could

not cure his cancer or delay its progression, he continued to ask me repeatedly, *"But shouldn't I be doing* something?"

The Spectrum of Responses to a Terminal Cancer Diagnosis

At first I could not understand why Uncle John was dismissing the unanimous advice of all his physicians, and I was furious at our family and his friends for supporting his "delusions." What was causing this breakdown in communication?

The answer, I later realized, could be found by analyzing our family's behavior using the framework of the emotional stages cancer patients often experience after they are told they have a terminal illness. Dr. Elizabeth Kübler-Ross first described these stages in her seminal book *On Death and Dying:* they include *denial, anger, bargaining, depression,* and *acceptance.* In this first book, Dr. Kübler-Ross cautioned that some patients do not experience all stages and that some experience them in a different order, or even simultaneously (e.g., anger and bargaining). She later expanded her conception of the emotional processes that occur as a person faces death, but this first formulation still provides a useful framework for understanding the spectrum of patients' feelings.

I began to notice that our family members and friends were going through these same emotional stages, but we were each going through them at a different rate. Our problems of communication arose because we were almost never in the same stage of the process at the same time. (I suspect that some of us who care for patients with far-advanced disease also go through these stages to some degree, and a similar mismatch in stages may compromise our ability to understand patient and family goals.)

In fact, my uncle was not *denying* that he had cancer (*What do you mean I have cancer? I just came here for a check-up and now you tell me I'm going to die!*); he was denying the grimness of the prognosis. Despite his symptoms and debility, he simply could not accept that he might not get entirely better after radiation therapy, could not be cured, and was likely to die.

John's *anger* manifested later. Anger can be directed at God, at the doctor, at the patient himself *(Why didn't I get that colonoscopy?),* or, in Uncle John's case, at my husband, Fred (not his real name), who was unlucky enough to be the one to tell him something he very much wanted not to hear. During a phone call, Uncle John repeatedly asked Fred to tell him his prognosis. So Fred finally did. *"Fred,"* Uncle John bellowed, *"What are you telling me? That I'm not going to make it to Christmas?! That's only six months away! Who died and made you king? You're not even a doctor! How dare you tell me such a thing!"* And he slammed the phone down.

We are all familiar with what is likely to happen to the bearer of bad news, and thus I might have expected this response from my uncle. But I did not expect it from the family, too. As we soon discovered, they were also in denial—less than he was, perhaps, but more so than we were—about Uncle John's prognosis. They were furious that we had presumed to tell him that he might die of his illness in a relatively short time. There were several suggestions that my husband was an unfeeling brute who had recklessly removed whatever hope my uncle might have had left.

Unlike the other relatives, my husband and I had already passed through the first two stages of reaction to a terminal prognosis—*denial* and *anger*—and were even past *bargaining (if he goes through all his treatments and is a good patient, the cancer will miraculously disappear).* We were now experiencing a little *depression* and *acceptance.* Because we had accepted Uncle John's grim prognosis and had begun grieving, my husband and I were focused on making his remaining days as comfortable and rewarding as possible. And we wanted to be sure he knew time was short, so he could do the things people do when they're dying while he could still think relatively clearly. The rest of the family were still in a bit of denial and were not ready to talk about such matters. They were still focused on fighting his disease and were urging him to seek treatments that might at least delay the disease's progression.

My uncle, though still not sure about his ultimate prognosis, had accepted that his tumor was unlikely to respond to any antineoplastic chemotherapy. By insisting otherwise, family members were denying him an important avenue of support. Instead of letting him share with them his daily progress in overcoming the side effects of radiation and dexamethasone, they were making him feel worse by implying that he wasn't doing everything possible to obtain a cure (or to cure himself).

The Effects of Distance in Space and Time

An additional principle was operating here, one that is probably familiar to those of you who have taken care of patients whose immediate relatives live at some distance: the intensity of the therapy family members demand varies directly with their distance from the patient and with the length of time since their last visit.

My uncle lived in Massachusetts. His relatives in Florida, who had not seen him for several years, wanted everything done and no expense spared in prolonging his life; those who lived in Washington, D.C., demanded somewhat less

intensity of diagnostic and therapeutic interventions; we, who had seen him most recently, knew hospice care was most appropriate.

Once I understood what was underlying our various positions, I was able to explain to other family members why their efforts were counterproductive and to convince them to stop hounding my uncle to seek out a miracle cure. His anxiety decreased when they stopped raising questions that he thought had already been answered satisfactorily. He sought psychological counseling to help him deal with his overwhelming situation and focused on the remaining goals he wished to achieve before he died.

Isolation: An Unintended Consequence of Protection

As it becomes clearer that the final months are approaching, patients and their families often seek to protect each other from the impending loss.

The Case of the Disappearing Walls

One morning I had to tell Simon Babar, a patient with colon cancer and extensive metastases to his liver, that the chemotherapy no longer appeared to be working—the metastases in his liver had become larger. I added that no other therapies were likely to stop the tumor from growing and that I felt he was likely to die within the next few months. Simon said that he was not really surprised, because he had been feeling weaker and had almost no appetite. He said he was OK with the news but asked me not to share this information with his family.

Similarly, when I had to inform a family of bad news before I'd been able to talk with the patient, some asked me not to share the information with the patient, going so far as threatening to sue me if I did. Whether it is understood as such, in both types of situations, the underlying motivation is to protect loved ones. Patients and families are often unaware of this protective instinct; they are worried that if the truth were known, either the family would decompensate from grief or the patient would "give up" and die precipitously.

Rather than betray Simon's trust, I tried to help him understand that he would be hurting his wife and children more by keeping the grim prognosis from them than by telling them. I said something along the following lines:

I realize that you want your wife and children to be spared the pain that you're now feeling. And I can certainly understand that impulse. But your family is pretty smart

and must have a sense of what has been going on. Your weight loss, your increased pain, and your profound weakness are hard to ignore. By pretending they're not happening, you make it impossible for your family to talk with you about what they're feeling. They are unlikely to initiate the conversation because they want to protect your feelings as much as you want to protect theirs.

By shielding them, you are isolating them from you, leaving them to face their fears and grief alone. They want to comfort you, to help you set and reach goals for the time you have left. There may be things they want to say to you, and you to them, that have been hard to say before but would be easier to say now.

When you don't talk to them about something as important as the fact that you're dying, it's as though you are building a room around them without doors or windows. But when you tell them how serious things are, you are letting them know that it's OK to talk with you about it. You create a door in one of the walls through which they can come out and join you. Then, instead of being isolated from your family, you can share your love and concern and can comfort each other.

Simon thought over what I'd said, then asked me to be present when he shared the information with his family, who were waiting outside his room. He said that he hadn't wanted me to tell them because, somehow, if he did not talk about it, nothing would change. He did not want his family feeling sorry for him, treating him differently, or being sad because he was dying. But he now realized that they probably did know that his illness had gotten much worse, and he welcomed the chance to get everything out into the open. Before I let in his wife and children, he joked, *"Go ahead and open the door, doc. I'm ready to blow down all four of those lousy walls!"*

Avoiding Patient Abandonment

Sometimes a physician can unwittingly be the source of unnecessary distress to a patient with far-advanced cancer. The Smiths' story is a sad example of how good intentions can be subverted by poor communication skills.

Abandonment

Mr. Smith was treated for several years by his local oncologist, Dr. Verna, for metastatic prostate cancer. When it stopped responding to the standard therapies, Dr. Verna referred him to Dr. O'Brian, an oncologist at an academic cancer center one hour away who specialized in experimental therapies for prostate cancer. Mr. Smith underwent several trials at the cancer center but had not been back to see Dr. Verna for over a year when he and his wife reappeared, crestfallen.

They told Dr. Verna about their last visit with Dr. O'Brian, and repeated what she had said, "word for word": *"Mr. Smith, your last bone scan showed progressive disease,"* she had told them. *"I'm sorry, but there's nothing more I can do for you. I think it would be better if, in the future, you went back to Dr. Verna for your care."*

It is likely that Dr. O'Brian thought she was doing the Smiths a favor by sending them back to their local oncologist and not forcing them to make the hour trip each way to the cancer center. But *the way* she told them upset them very much.

The Smiths told my friend that they had been crushed by that last visit: not only was the cancer progressing, but there was "nothing more to be done." Think how much better Mr. Smith would have felt if Dr. O'Brian had at least thanked them for their help in advancing the field by participating in the cutting-edge clinical trials and offered to call Dr. Verna for them to ensure there would not be anything missed during the transition. That would have made her reasons for referring him back much clearer and would have spared their feelings.

Dr. Verna reassured the Smiths that he was delighted to resume Mr. Smith's care and that he could do a great deal for them. He suggested that although Dr. O'Brian was an expert in the aggressive treatment of the cancer, he could offer therapy that was just as aggressive to control any cancer-related symptoms that arose at this stage of the disease. He also encouraged them to tell him more about how they had felt when asked to leave the cancer center.

The Smiths admitted that they had felt abandoned, worthless, and hopeless. Under the same circumstances, your patients might reveal anxiety or similar signs or symptoms of depression. If these are severe, you may need to refer them to a psychologist, psychiatrist, pastoral counselor, or social worker with psychological training.

It may take several months, but you will most likely be able to reestablish the hope and trust of patients like the Smiths. By continuing to show sensitivity to their feelings and by meticulous attention to their medical as well as their psychosocial and spiritual concerns, you can help them regain feelings of worth and hope and can demonstrate the array of effective therapies remaining for them.

Prioritized Symptom Lists

If you are an oncologist who trained before palliative care was part of the program, or if you're not an oncologist, when you assume the care of patients with

advanced cancer, you may find yourself wondering where to concentrate your efforts. Patients and their families may come with a seemingly insurmountable symptom list, including physical, social, spiritual, and emotional problems. Dr. Russell Portenoy (currently professor of neurology at Albert Einstein College of Medicine and chairman of the Department of Pain Medicine and Palliative Care at Beth Israel Medical Center in New York) and other members of the Pain and Palliative Care Service at Memorial Sloan-Kettering Cancer Center taught me how to prioritize these complaints.

Physicians, families, and patients first determine which symptoms are most troublesome, which are likely to respond to therapy, and which, if any, aggressive diagnostic evaluations and therapies the patient is still willing to accept. They use this information to rank the problems in order of both import to the patient and ease of reversal (Portenoy 1993). Using this "prioritized symptom list" as a guide, your efforts can be focused on controlling the most distressing and the most reversible problems.

The Patient's List

As Mr. Smith's prostate cancer progressed, his symptom list included:

- Pain
- Dry mouth
- Constipation
- Weakness

Dr. Verna reassured Mr. Smith that his pain could be relieved to a degree that would be satisfactory to him. With oral or transdermal medications, you can expect to relieve the pain of 90 percent of your patients with cancer. Constipation, whether due to hypercalcemia, inactivity, or opioids, is even more likely to be entirely relieved. The mouth dryness will lessen if the patient discontinues medications with anticholinergic properties (such as diphenhydramine) or adds agents that stimulate saliva production—pilocarpine or sour candies, for instance. (Later chapters provide more details on the therapies that are effective for these complaints.) Unless the weakness is caused by anemia, however, it is likely to be more difficult to reverse.

In that case, what can be done? I'd tell Mr. Smith that I was confident we could treat the first three symptoms successfully, but I'd admit that his weakness was less likely to be reversible. Patients usually appreciate such frankness and are often willing to redirect their energy toward ameliorating symptoms that are likely to respond to therapy.

The Family's List

The family's list is rarely as straightforward as the patient's. Underlying the problems they report are the hidden concerns and unasked questions that are usually equally troubling and even harder to address. One family with such concerns was the Hermans.

Unspoken Family Expectations

Mr. Herman was a 65-year-old man whose metastatic lung cancer had progressed despite therapy. He had the same complaints as Mr. Smith (pain, dry mouth, constipation, weakness), but he seemed very satisfied with the treatment regimen I had instituted. I looked forward to his weekly visits. But at one visit, his wife and daughters accompanied him, and they were by no means pleased with his progress. The daughters detailed their concerns:

Dad is not eating enough and is spending most of his day in bed because he's so weak. We don't understand why you haven't given him something to increase his appetite, or maybe put a feeding tube in his stomach. If he got more food, we're sure he'd get stronger and feel much better. Also, Mom tells us that he keeps her up half the night, helping him to the bathroom or worrying that he needs something as he tosses and turns. She thinks this means he's still in pain, though he's taking the medicine you gave him. We know there's nothing that will stop the cancer, but he lies around in bed all day. We bring him his favorite foods, but he only picks at them. Can't you do something?

As I listened, I mentally created what you might call "the family's priority list."

The Patient's List	*The Family's List*
• Pain	• Weakness
• Dry mouth	• Lack of appetite
• Constipation	• Sleeplessness
• Weakness	• Pain

As you can see, the family's priority list differs significantly from Mr. Herman's. Pain and weakness make it onto the list, but their order of importance is reversed. Mr. Herman's lack of activity was not troublesome to him, but it was severely distressing to his family, as was his sleeplessness. He had *no* complaints of hunger or thirst, and yet his family was asking me to put a feeding tube in him. How was I to meet his family's needs without subjecting Mr. Herman to unnecessary procedures or medications?

The key was to understand the hidden concerns that led to such disparate priority lists. What were the underlying causes of the family's distress? Dr. J. Andrew Billings's *Outpatient Management of Advanced Cancer* offers useful answers in its discussion of the concept of *attribution*—what meaning the family attributes to the patient's actions, rather than what the patient's actions actually mean. Mr. Herman did not eat because he wasn't hungry, but his family was attributing his failure to eat to a rejection of the food they prepared and, by extension, a rejection of the people preparing it. This same reaction manifests in families in which children have made food choices that differ from those of their parents. Meat-eating parents of vegetarian children are often outraged at their offsprings' choice of diet. Why? Not because the diet they have chosen is unhealthy but because, in rejecting their parents' food choices, the children are rejecting their parents and their values.

Mr. Herman is simply not hungry—but his family feels rejected and left out. They also attribute his failure to eat to his "giving up." It feels to them like the first step toward the eventual abandonment his death will bring. They want me to prevent or at least delay this. His staying in bed only serves to reinforce their conviction that he is giving up or, in other words, that he is leaving them before they're ready for him to go. And they cannot bear that.

Once I understood these hidden concerns, I could address them, rather than just deal with the requests themselves. As a palliative care physician, I often have conversations like this with families. But as his oncologist, I could also have said:

I know it must hurt when your dad doesn't eat much of the foods you prepare especially for him. But as he's told you, he's really not hungry or thirsty. It's very common for people who have as much cancer as your dad does not to feel hungry or thirsty, and to get enjoyment from much less food than we need. But rejecting your food doesn't mean he's rejecting you—he loves you and wants to be with you as long as he can. He is getting weaker, but that is because his cancer is getting worse. Putting a feeding tube in him won't make him live any longer, and it's likely to make him less comfortable in the time he has left. He can already eat anything he wants, and even though he doesn't eat a lot of what you bring him, knowing you make or bring anything he asks for really makes him feel loved and special.

To families for whom "giving up" seems to be an important issue, I might also say:

I know it must seem as if he's giving up—as if he's leaving you—and that hurts, too. But he's fought this cancer a long time, and he's tired of fighting now. He loves all of you very much, and that hasn't changed just because he can't fight anymore. Let's all

concentrate on helping him have everything he wants and on helping him be as comfortable as possible for as long as he has left.

In my experience, this difference between patient and family priority lists is the rule rather than the exception. Thus it was common for me to have discussions similar to those described above. Almost always during such a talk, family members began to acknowledge their feelings and to overcome their denial of the seriousness of the patient's condition. Requests for medications to increase appetite or for placement of a feeding tube disappeared, as did the need to call in the hospital ethics committee.

It would have been simpler for me to accede to the Herman family's requests to refer him for a feeding tube, but to do so would have been a disservice to Mr. Herman—and to his family as well. I would not have discovered or helped them deal with their feelings of rejection and grief. If they never realized that these feelings were underlying their requests to me, their final days with Mr. Herman might have been marred by their unspoken anger at him, and their grieving after his death would have been unnecessarily complicated by this anger as well. Uncovering and thereby eliminating these feelings optimized family members' interactions with him in his final days and improved their ability to deal with his eventual death.

The Physician's List

Errors of commission. As physicians we are not immune to creating priority lists that differ from both the patient's and the family's. We have had personal experiences that make us feel we must offer certain treatments to patients, whether or not they express a need for them. This became clear to me when I was working with a surgical chief resident who had admitted one of my patients.

Misdirected Efforts

Mr. Jackson had colon cancer that was metastatic to his peritoneum and liver. He had been admitted to the surgical service for a possible small-bowel obstruction. The obstruction responded to conservative measures, but Mr. Jackson had to remain in the hospital while awaiting placement in a nursing home.

The surgeon complained to me about Mr. Jackson's poor oral intake. I explained to him that the patient had told me he was comfortable since the obstruction had resolved and that he was eating all he wanted. To my surprise, however, when I returned three days later from a conference, Mr. Jackson had a feeding tube in place.

I sought out the surgeon and asked why, despite my express wishes to the contrary, he had placed a feeding tube in Mr. Jackson. At first he reiterated his concerns about Mr. Jackson's poor oral intake, but finally he explained his real reason. It seems that his own grandfather was dying of esophageal cancer and was unable to swallow anything. The surgeon's father was therefore delivering medications via suppository, which the surgeon found extremely degrading. He told me vehemently, *"No other family is going to have to go through what my father is going through!"*

I gently reminded him that my patient had a totally patent esophagus and could swallow perfectly well—he just had no appetite. The surgeon rather sheepishly agreed that Mr. Jackson hadn't needed the tube and that he did not realize how much his own family situation had clouded his judgment.

Errors of omission. In addition to errors of commission (such as inserting an unnecessary feeding tube), our own needs can also lead us to equally serious errors of omission. In Chapter 1, for example, I reviewed the barriers that prevent us from discussing advance directives with patients with far-advanced disease. It is even harder for many of us to participate in the emotionally intense and often draining care of patients who are in their final months.

Eric Cassell, in *The Nature of Suffering and the Goals of Medicine* (2004), offers insights into the factors that prevent physicians from appreciating the needs of dying patients. The initial obstacles appear during medical school, where we learn what he calls "The promise of science: to know the disease is to know the illness and its treatment" (p. 20). He notes that "many doctors—perhaps most people—still believe that different persons with the same disease will have the same sickness" (p. viii). But a disease such as pneumonia, he explains, can cause different illnesses in different people. Moreover, science is value-free and objective, but doctors are in the business of treating *people,* who are value-laden and, by their very nature, subjective. A sick person, he says, is the subject not the object of care. There is no population for whom this is more true than the dying.

But how are you to know your patients' values? Some of you are lucky enough to have the luxury of longitudinal relationships with your patients. You may come to know their values through the choices they make as you treat their various acute medical problems or guide them through their cancer therapies. Are they risk-takers? Is quality of life of paramount importance, or quantity? How did they tolerate treatment-related side effects? Did incapacity affect their sense of self-worth? And so on.

This knowledge is invaluable for anyone who seeks to understand how best to serve their dying patients and their families. You must elicit the information through careful questioning of your patients about the goals they wish to achieve and how they hope to function, and you must take care not simply to substitute your values for theirs.

Moving Forward to "Comfort Care"

Making the Transition

There comes a time when the burdens of antineoplastic treatment begin to outweigh the benefits. Even when the treatment itself has few side effects, the frequent trips for therapy, or the constant monitoring of blood counts and renal and hepatic function, become a drain on precious energy reserves. Maintaining a focus on treatment without letting patients know clearly that only months of "good time" remain is likely to result in their not using this precious time to complete personal and professional goals. How can patients and their physicians make this transition and avoid risking their relationship? Sara Bloom's story is illustrative of the dilemma.

Sara was a 53-year-old widow with a PhD in psychology. She had been diagnosed with colon cancer five years before, received adjuvant chemotherapy, and for the last three years had received treatment for metastatic colon cancer. Her tumor had slowly progressed despite a series of agents, and she was now on a daily oral regimen that required monitoring of her blood counts and renal function. Her monthly taps of ascites were now needed every two weeks, and her fatigue was increasing despite erythropoietin and red blood cell transfusions about every six weeks. Sara also was quite sensitive to the cognitive effects of the opioids she needed for pain control. Dr. Olinsky, her oncologist, asked our palliative care team to work with Sara to identify a regimen that would be less sedating. Sara had three adult children, one of whom always accompanied her to her office visits.

During a follow-up visit with all of us, Dr. Olinsky told Sara that her recent CT scan showed slight progression. Dr. Olinsky added that he thought Sara should stop her current therapy and take a break for a while to "regain her strength," after which they could consider adding something new. Sara was very upset. She angrily accused Dr. Olinsky of abandoning her now that she was no longer eligible for experimental therapy trials. She directed her daughter to wheel her "out of here" and, glaring at Dr. Olinsky and me, said, *"What do you all expect me to do now . . . just sit by the window waiting to die?"*

The work of Schou and Hewison (1999) can help us understand Sara's outburst. These sociologists studied patients receiving radiation therapy as well as their families. The families were negotiating the care systems for the first time, and Schou and Hewison tried to determine which elements of the experience contributed to or detracted from the patients' quality of life. Their insights are equally applicable to patients like Sara who are undergoing other antineoplastic regimens.

Before they begin treatment, patients usually have a variety of plans for the future. Schou and Hewison suggest that to understand what is happening, we think in terms of calendars by which patients and families run their lives: the *sociocultural calendar,* which includes holidays like Thanksgiving, Christmas, and Passover; the *personal and private calendar,* which includes birthdays, anniversaries, weddings, and graduations; and the *life calendar,* with church, soccer practice, and play dates. In addition to these events of daily living, the life calendar also includes plans for achieving goals in the realms of work and relationships.

Once treatment starts, Schou and Hewison argue, all these calendars are superseded by the *illness calendar* and the *treatment calendar.* The *illness calendar* begins during diagnosis and continues as long as the patient requires medical check-ups. Of more immediate concern to patients and families, however, are the *treatment calendars* which they create each time a patient begins a new therapy. Patients and their families vest the current treatment calendar with the magical power to bring about a cure. Any disruption in that calendar is therefore very distressing: they strive to complete the treatments "on time" so that all will be well. When white blood cell or platelet counts are too low, patients see the nutritionist and ask what they can do to "get back on schedule."

You may know that the schedule is not so important for palliative treatment regimens, but patients do not know this, and they rarely ask to delay a treatment in order to feel better for an important event. For example, offers to delay chemotherapy until after Thanksgiving are often met by patients with a puzzled refusal. It is as though you were thoughtlessly jeopardizing the patient's future.

Dr. Olinsky and his team needed a plan for when they resumed Sara's treatment. To prevent a recurrence of her feeling of abandonment, they needed to encourage her to reintegrate into her daily life the activities that were meaningful before treatment began, the things that filled up her *personal and private* calendars. Sara and her family could work with his team to schedule treatment sessions to accommodate important family events or holiday celebrations. When he reinitiated treatment, Dr. Olinsky would reassure Sara and her children that minor alterations in

the schedule would not affect the efficacy of the treatment. In this way, Dr. Olinsky would be able to help Sara rebuild her *personal calendar*, and as that calendar filled up, to help her begin to adjust to the knowledge that for whatever time she had remaining, he could accommodate her schedules.

In the meantime, we encouraged Sara to use the energy she had during this break to think about which important events she would like to be a part of, and how to create her legacy. Some patients hope they can participate in a child's graduation, or be present for the birth of a grandchild. For Sara, the event was her daughter's wedding, planned for four months hence, although the odds were that she would not survive that long, or if she did, would not have the energy to enjoy it. We therefore urged Sara to make use of her time before the next treatment started to ensure that she would have some presence at the wedding, in case it could not be the presence she wanted. We helped her children make videos with her, including one in which she narrated the family scrapbooks and other photos and videos as part of her wedding gift.

Our palliative care team often suggests that patients with young children or grandchildren consider writing letters to them for events far into the future, or create or purchase gifts that will embody their love and ensure that they will be there in spirit. For patients who assure us they will be there in person, we reply that if all goes as they hope, the children will simply have extra gifts to enjoy, knowing they were in the patient's thoughts even when things looked darkest.

As disease progresses despite ongoing treatment, patients who, like Sara, have begun to reengage in non-treatment-related activities and have developed a broader relationship with their oncology team are more likely to understand later that you are not abandoning them when you tell them that the burden of another therapy is much greater than the potential benefit. When Dr. Olinsky next proposes that therapy be discontinued, Sara will be less likely to complain that for her, stopping treatment was "waiting around to die," because she will have found other activities to fill her days.

This shift from antineoplastic treatment to comfort-focused care is the last important hurdle to overcome as you and your patient approach her death. Discussions about this shift often take place when the patient is hospitalized, when it is clear that further therapy directed at the cancer, an underlying infection, or anything other than comfort is no longer appropriate. House officers and physician assistants have not been trained in these areas and are usually unsure of how to approach the family with their concerns about the appropriate level of care; they can benefit from the guidance of a more experienced clinician.

You do best when you express yourself by using words that convey concern rather than words that imply a lack of concern. You want to provide *comfort* and *care,* yet you might speak only in terms of *withdrawing* care. Ensure, therefore, that your conversations with patients and their families don't focus on what you don't want to do; focus rather on what you do want to do.

Families are unlikely to realize that interventions that were previously helpful no longer are, or that close monitoring of blood tests no longer provides information needed to make the patient more comfortable. Phrases such as, "*It's no longer indicated*"; "*We want to* stop *the antibiotics and blood transfusions*"; or "*We won't be doing any more tests,*" therefore, may lead the family to conclude erroneously that useful interventions are being discontinued or that *all* care is going to be stopped. Families can easily focus on the *stop* part of the message and respond, "*But we want everything done. How can you deny our father the care that he's entitled to?*"

Substituting phrases such as the following conveys a more accurate idea of caring and support and enhances the likelihood that the family will agree that comfort care is best for the patient: "*We want to care for your father as you would at home if you had all the help we do here. We'll do all we can to make sure he is comfortable, and we'll only do things that will make him feel better.*"

It is also important, before proceeding, to evaluate the burdens and benefits of each diagnostic test and of each treatment. The burden/benefit ratio will vary depending on the patient's goals and values, her mental and physical condition, whether the problem is likely to be reversible, and how far the underlying disease has advanced.

As you would expect, these burden/benefit dilemmas become more frequent as the disease progresses. For some patients with shortness of breath from a pleural effusion, a chest tube is the answer. For others, oxygen and morphine given at home provide more appropriate palliation. Two patients, one with newly diagnosed non–small cell lung cancer and the other bedridden with widely metastatic, refractory breast cancer, might have the same cancerous invasion and pathologic fracture of the T10 vertebra, with epidural extension of tumor but no compression of the spinal cord. Neither has been irradiated in that area, and thus both are candidates for surgery and radiation therapy or radiation alone. For the patient who has no other complications from lung cancer and has an active life and no other sources of pain or disability, the choice is clear—the spinal metastasis should be treated aggressively (i.e., fractionated radiation therapy or resection followed by fractionated radiation therapy) to prevent the spinal cord compression that is otherwise likely to follow. But for

the patient riddled with multiple painful bone metastases from refractory breast cancer, pain medication alone or a single treatment of radiation therapy may be preferable.

PRACTICE POINTS: MOVING TO COMFORT CARE

- Convey concern.
- Reassure the patient and family that you will do everything possible to keep the patient comfortable.
- Consult with the patient and family to determine the burden/benefit ratio of each test and treatment.
- Work with them to tailor the diagnostic and treatment plan toward achieving and maintaining an acceptable quality of life.
- Explore the patient's and family's religious beliefs about the significance of accepting comfort care.
- Reassure the patient and family that you will not abandon them.
- Be open to discussions of psychological, financial, spiritual, and existential concerns.
- Readily refer patients and their families to palliative care, to hospice, or to individual professionals who can address these concerns.

In less clear cases, how do you know which therapy is appropriate? You review the overall condition of the patient as dispassionately as you can and, whenever possible, make the patient an active participant in the discussion. This enhances the chance that you'll be able to tailor all evaluations and treatments to achieve a quality of life that is acceptable to your patients.

Impact of Religious Views

An exploration into the patient's religious beliefs is an important prelude to suggesting that the goals be shifted to those of comfort-focused care. Sometimes you will discover a deep faith in a loving God who is expected to "take me home." These patients are often happy to accept care that focuses on their comfort. Others, however, hold tenets that make the transition almost impossible.

Some patients, for example, feel that their religion prohibits them from accepting any course of treatment that might shorten their life. As I reviewed in Chapters 1 and 2, most Christian, Jewish, and Islamic teachings support the right of the patient to refuse futile and excessively burdensome treatments and

to accept pain relief even if they risk an earlier death. But some Orthodox Jewish rabbis and some Evangelical or Pentecostal Christian sects regard all God-given life as sacred, and nothing that would diminish it by even a moment is acceptable. Patients of those faiths might feel that accepting comfort care is tantamount to admitting that they no longer have faith in God. Should this be the case, it may be helpful to confer with the patient, the family, and their spiritual leader to clarify the acceptable goals of care. In the worst case, if you do not feel you can abide by a patient's wishes, you may have to identify another physician who can.

A patient's beliefs about the nature of an afterlife and the effects of one's past activities on it can also enhance or inhibit the acceptance of death and consequently can affect the patient's ability to accept comfort measures. Religious Christians or Muslims who expect to be judged and sent to heaven or hell based on their actions, or Buddhists, who believe that the sum of the worth of their deeds (karma) will determine the nature of their reincarnation, may fear death if they judge themselves to have led a life that will be found morally wanting. They will seek any treatment to defer a death that is terrifying to them. In Chapter 5 you will find questions that can help in determining whether patients have unresolved, distressing, existential, or spiritual concerns that prevent them from accepting the reality of their medical situation.

Readdressing Resuscitation

I work with many patients who have far-advanced disease but choose to be resuscitated when they die, despite even their oncologist's explanations, in advance, that they will end their days in an ICU.

Young parents. As you might expect, the concerns that lead younger patients (especially young parents) to refuse to name a health proxy or consider DNR status usually differ significantly from those of older patients.

Young adult patients (35 years old or younger) are often just beginning to have their hard work pay off in successful careers or growing families. They seem to be trying to make sense of their short lives, or wondering how they can possibly leave their children. Some have no religious tradition that can help them make sense of what is happening to them. For patients with existential distress, we can offer to help them tell their stories, to bring meaning to the short lives they have had, as I discuss in Chapter 9.

Young parents, especially single parents, present a heartrending challenge. We always explore whether we can help them with concerns about their children. We try to ensure that the children are offered counseling, at least from

their school counselors, who should be aware of the parent's serious illness. Dr. Paula Rauch, professor of psychiatry, director of the Cancer Center Parenting Program and chief of the Child Psychiatry Consultation Service at Massachusetts General Hospital, developed and directs the PACT program at the hospital. PACT is for children with a dying parent or for parents with cancer who need help learning how to talk with their children about their illness and even their impending death. Rauch's guidelines for clinicians who work with these parents and their children include six steps.

PRACTICE POINTS: PARENTS WITH YOUNG CHILDREN

- Learn about the children.
- Maximize the child's support system.
- Facilitate honest communication about the illness.
- Address common questions.
- Prepare for hospital visits.
- Encourage parents and children to say good-bye.

(From Rauch et al. 2002)

"*(1) Learn about the children.*" Start with something simple like asking parents to tell you about their children, including their ages and how they coped with previous personal or family challenges.

"*(2) Maximize the child's support system.*" A mainstay of a support system for children is maintaining their normal routine. Help the parents identify who among their family and friends can help keep the children's schedules as close to normal as possible, including sleeping, eating, school, friends, and out-of-school activities. If the ill parent encourages the children to form relationships with these nonparental friends, the children won't feel disloyal in doing so.

"*(3) Facilitate honest communication about the illness.*" Parents need to spend as much time as is needed to ensure that their children have all their questions answered in a way that is appropriate for their ages. Children from 3 to 7 years old may mistakenly feel that they are the cause of their parent's illness. These children may be expressing their guilt by "anxious, inhibited behavior or outbursts of angry, oppositional behavior." Their parents need to ask the children what they think caused the cancer, so they can correct their misunderstandings. Young children do not understand that death is permanent, so death need not be part of the discussions while the ill parent is alive. Older children (7 to 12) may also fear that their behavior contributed to the cancer, and they also

need to be reassured that "the cancer is not contagious and that not all cancers are caused by cigarette smoking." They do know that death is permanent, and so they may need to discuss their fears and concerns about their parent leaving them. Children should be encouraged to share any stories they have heard but don't understand, and to ask any questions they want to. Parents, however, have to be careful to understand what the real question is, and should feel free not to answer every question right away. Saying, "That is an important question. Let me think about it," is fine, so long as you remember to give an answer at a later time.

"*(4) Address common questions.*" Parents often ask Dr. Rauch, "What do we call the illness?" She encourages them not to use euphemisms, but rather to name the cancer specifically. Calling it a "boo-boo" or bump may scare and confuse children who themselves have had many a boo-boo or bump. Parents also ask, "How much should we share with the children?" Dr. Rauch says, "Assume that whatever the adults are discussing will be heard by the children." They are likely to feel more frightened by being left to interpret the information alone than if they are present, informed, and can be comforted should they show distress. Another question from parents is, "Should I make my child talk about the illness?" Although it is important to let children know that a parent is available to talk if they want to, Rauch advises parents to let their children initiate the discussions. "Are you going to die?" is, Rauch says, "the question most commonly feared by parents." She advises parents to ask about "specific worries about what would happen if the parent died" (such as whom the children would live with), and to share that although the illness might be fatal, they're doing all they can to live as long as possible and as well as possible.

"*(5) Prepare for hospital visits.*" Children should be allowed to visit the hospital if they want to, except when a parent is confused or agitated, which a young child is unlikely to understand. But they need special preparation for what they are about to see, including a discussion of their fears and expectations, and someone to take them who can leave when the child is ready to leave. After the visit, children should be asked to discuss any parts that were difficult or enjoyable, or were different from what they expected. For children who do not want to visit, a family member or other trusted adult can help them communicate with the ill parent by preparing letters, drawings, or other gifts, lending the parent one of the child's own best-loved toys (such as a stuffed animal), making videos, or talking on the phone or videophone.

"*(6) Saying goodbye.*" Rauch says, "If one's children know they are loved, and why they are loved, there is usually no need to say the word 'goodbye.'" But she encourages parents and their children to say a last "I love you" in person

whenever possible. If necessary, a child can say it to a parent in a coma, or after the parent has died. Children should also be given "a road map for the grief process ahead," and the surviving parent can help the children feel comfortable about going on with school and other activities after the death by encouraging them to talk about what they have been doing, just as that parent did before the death.

Using these guidelines, clinicians can often help parents make the plans needed for care of their children when they are gone. Although parents face their deaths with undiminished sadness, they are able to say what their children need to hear. Sometimes, when appropriate plans have been made, these patients will see the benefit of appointing a health care proxy and, when appropriate, of asking not to be resuscitated.

Recognizing the Miracle

Jonathan was a 45-year-old mentally disabled man with recurrent, refractory lymphoma that was progressing rapidly and causing increasing respiratory distress from pleural effusions and interstitial disease. The attending physician had tried repeatedly to obtain consent for a DNR/DNI order from Jon's health proxy, his mother. She and his aunts and uncles were always at his side, and when our palliative care team met them for the first time, they were clear that they had a very strong belief that Jon would be saved by a miracle. They were also clear that they did not want to discuss the DNR question further, intimating that we were trying to deny Jon the care he deserved. Jon was so ill that he was not able to communicate verbally with us, though his family felt he could communicate discomfort to them.

The majority of the public thinks that miracles can save even patients in a persistent vegetative state, and that a divine intervention can save a person whom physicians think is beyond saving. A large majority of the believers feel that God's healing acts come through physician intervention. Unfortunately, our prognostic estimates do not sway these families. They weigh the physician's judgment against "1) their own knowledge of the patient's intrinsic qualities and will to live; 2) their observations of the patient; 3) their belief in the power of their support and presence; and 4) optimism, intuition, and faith" (Widera et al. 2011).

Our team decided it might help our relationship with the family if we were careful to demonstrate how much we did care for them and for Jon. We knew that we needed to show the family that we could see and hope for what they were seeing

and hoping for. If, in our frustration and concern that we might have to resuscitate Jon, we persisted in trying to get Jon's family to agree not to resuscitate him, we would have set up a polarity that did not need to exist. We would have allowed their anger at us to prevent them from seeing that Jon was dying.

We began twice-daily meetings with family members to assess their understanding of Jon's condition and to tell them about the measures the medical team was taking and any plans for studies or changes in his regimen. We included all his family caregivers in this widened focus of care, asking how they were doing, what their hopes and fears for Jon were, and whether they thought Jon had any spiritual needs that were being unmet. One of their hopes was that Jon would come home, so we introduced them to the hospice liaison, reassuring them that they need not opt for DNR to enroll. That was news to them, and they were very interested in the support hospice programs could offer.

As we expected, Jon's condition suddenly worsened, and he was unable to communicate in any fashion. His attending physician received a 1 a.m. phone call from the covering resident, saying that unless Jon was intubated very soon, he would die. She told Jon's mother, who was staying in the hospital with him, of the impending crisis and for the first time asked her whether she should intubate him. Jon's mother calmly and sadly refused, adding that the family had noticed the change in Jon that day. *"The miracle we asked for has come,"* she said tearfully. *"He is peaceful at last."*

We can sometimes gain the trust of families who are waiting for a miracle by providing meticulous patient care, respecting their views, and attempting to fulfill their needs. When we let go of the "DNR agenda," our compassion can shine through. Families who are not spending their time fighting us can, with assistance from their pastor or social worker, reflect on what is best for their loved one and reconcile their loss and their beliefs. When the end nears, they and the health care team can arrive at the same place, albeit by different roads.

Older patients. Family concerns can also cause older patients to demand resuscitation. Some are the center of their family constellation, the matriarch or patriarch to whom everyone has turned for advice, validation, and love. They have directed careers, patched up marriages, managed divorces, run the family business, comforted angry teenagers, and made peace between generations. When disease overwhelms such a person and there has been insufficient time to delegate that role and its responsibilities, dying is not an option. Despite being told repeatedly by their trusted oncologist that resuscitation is futile, such patients

cannot accept DNR orders. For them, communication even while intubated is preferable to death.

Sometimes, through intensive work by the social worker with the family and the patient, the burden of leadership can be transferred to one or more family members. Encouraging family members to let the patient know that they will take care of each other, and that the patient's spirit will continue to guide them, can sometimes release the patient from the strongly felt obligation. When these older patients remain unconvinced, you may have to resuscitate them against your better judgment.

For other patients, it is a religious belief that is tormenting them.

Molly was a 77-year-old woman with end-stage breast cancer that had infiltrated her lungs to the degree that she required maximum respiratory support and was nearing the point of needing noninvasive positive pressure ventilation (BiPAP) or even intubation. We were unable to relieve any of her anxiety or insomnia with medications and relaxation techniques. Her concerns became clear only when we visited Molly with our chaplain.

In response to questioning, Molly said that she did believe in God but immediately burst into tears; she told us how she could not sleep because she saw the fires of hell that were going to consume her when she died. She declined to share with us what it was that she had done, but when the chaplain asked whether the God she believed in was a vengeful or a forgiving God, Molly said it was a forgiving God. The chaplain then told her the story of the prodigal son, reminding Molly that God waits for even the worst sinners to come back to him so that he can glory in their return. She asked Molly whether she would like to pray together, which they did. Molly did not sleep soundly that night, or come any closer to making an advance care plan, but she did begin a dialogue with the chaplain that led to a marked decrease in her anxiety and eventually to an improvement in her terror and her visions. And she was no longer afraid to ask her own pastor to visit.

Anticipating Family Concerns

Once family members have accepted comfort care as a goal, they want to be sure that they are doing everything possible to help the dying patient. Billings (1985) suggests that when a family experiences insecurity, it generally arises from a combination of factors: (1) anticipation of problems (i.e., anything they can imagine happening might indeed happen); (2) a sense of isolation combined with an overwhelming sense of responsibility; and (3) vulnerability and helplessness, which can lead to outrage and even anger.

BENEFITS OF HOSPICE CARE

- The hospice philosophy is to ensure the best quality of life for patients with terminal illnesses. Patients are eligible for the Medicare hospice benefit if they are eligible for Medicare and are expected to live for six months or less with the disease taking its usual course.
- Multidisciplinary team care usually takes place in the patient's home. The team includes nurses, social workers, nursing aides, chaplains, volunteers, and physicians (including the referring MD).
- Care is centered on the goals and values of patients and their families.
- Attention is paid to the physical, psychological, social, financial, spiritual, and existential causes of distress.
- All medications, equipment, and supplies related to the diagnosis for which the patient entered hospice, which are needed to maintain patient comfort, are provided.
- If needed, 24-hour home nursing or hospitalization of the patient for uncontrollable symptoms is available.
- Respite care for the patient in a nursing facility is available for about 5 days every month, if needed by the family.
- The patient does not have to request DNR to enroll.
- Support for the bereaved is routinely provided for approximately 13 months after the death.

To help a family avoid feeling insecure, Billings suggests that the medical team must (1) be available, (2) be consistent and dependable, (3) anticipate problems and rehearse responses, (4) elicit and address attributions (misinterpretations of what the patient's actions mean), and (5) offer reassurance, encouragement, and hopefulness. Hospice teams incorporate all these components in their plans of care. Their vision, as stated by the National Hospice and Palliative Care Organization, is "A world where individuals and families facing serious illness, death, and grief will experience the best that humankind can offer." The NHPCO model of hospice care is a model we all can follow: "Considered to be the model for quality, compassionate care at the end of life, hospice care involves a team-oriented approach of expert medical care, pain management, and emotional and spiritual support expressly tailored to the patient's wishes" (NHPCO 2013).

Rather than waiting until death is only weeks away, we encourage patients to accept hospice care as soon as we determine that they are likely to live for six months or less if the disease takes its expected course. Families and hospice

workers report that having this time to get to know one another enhances the hospice team's understanding of the patient's and family's needs and its efficacy in providing help during the last days. It is usually not difficult to determine when cancer patients are eligible for hospice, but for patients with nonmalignant terminal illnesses, this can be difficult. Medicare administrative contractors in each administrative region create local coverage determinations (LCDs), which are then approved by the national Center for Medicare and Medicaid Services (CMS). When I put "Hospice LCD" into my search engine, I found a number of links to "Hospice Local Coverage Determination (LCD)-CGS." The hospice eligibility criteria for Region 1, which are likely to be similar to the other LCDs, is given in Figure 4.1.* The levels of clinical care that hospice programs provide are described in Table 4.1. A helpful booklet, *Medicare Hospice Benefits*, describes for patients who is eligible for Medicare hospice and what the benefit entails. It is free from Medicare and Medicaid services (www.medicare.gov).

The home hospice team tries to anticipate problems and rehearse solutions. If, for example, the patient is likely to become delirious, they include appropriate medications (e.g., haloperidol) in the "hospice kit" the family has at home, teach the family how to identify delirium and how to reach the hospice nurse, and reassure them that the hospice nurses on call will tell them how to administer the psychotropic medications if needed. Hospice team members also reassure family members that they are doing a wonderful job, that they are special people for assuming this responsibility, and that by doing so, they are enabling their loved one to remain at home. They remind the family that they are not expected to be experts and that hospice personnel will be there to help.

Family members are understandably reluctant to leave the patient alone, so to help prevent family burnout, the hospice team will urge them to allow a friend, relative, or trained hospice volunteer to stay with the patient for an hour or two each day to enable them to get the break they need. They remind them that they must stay mentally and physically healthy and that full-time care of a patient with advanced cancer is exhausting. Hospice programs are also required to arrange for five days of respite care every month for each patient enrolled in the program, if the family requests it. The patient is cared for in a nursing home during this time, and caregivers can then go to a family reunion, graduation, or wedding or just catch up on some much-needed sleep.

*For those interested in more details, Chapter 9 of the *Medicare Benefit Policy Manual* describes the policies and procedures for clinicians and hospice administrators (www.cms.gov/Regulations-and-Guidance/Guidance/Manuals) and the *Federal Register,* volume 73, number 109, June 5, 2008, contains an update of the Medicare regulations.

General Guidelines

- Life-limiting condition
- Patient/family focus on symptom relief rather than cure
- Progression of disease(s)
- Evidence of weight loss; serum albumin <2.5 g/dl
- Symptoms & signs that paint a picture of decline
- Karnofsky or Palliative Performance Scale score <50%
- Dependence in at least 2 ADLs
- Need for frequent hospitalization, office or ER visits
- Progressive/unhealing stage III or IV pressure ulcers

Pulmonary Disease

- Severe chronic lung disease
  - Disabling dyspnea at rest, poorly responsive to bronchodilators
  - FEV1 after bronchodilator <30%
- Progression of end-stage pulmonary disease
  - Recurrent pulmonary infections
- Hypoxemia at rest, on room air: pO_2 <55 mmHg—or O_2 sat <88%
- Right heart failure secondary to pulmonary disease
- Unintentional progressive weight loss >10%
- Persistent resting tachycardia

Renal Disease – Acute Renal Failure

- Patient is not seeking dialysis or transplant
  - Creatinine >8 mg/dl(>6 mg/dl for diabetics)
- GFR <10 ml/min
  - Creatinine clearance <10 cc/min(<15 cc/min for diabetics)
- Co-morbid conditions

Renal Disease – Chronic Renal Failure

- Patient is not seeking dialysis or transplant
- Creatinine clearance <10 cc/min (<15 cc/min for diabetics)
  - Creatinine >8 mg/dl (>6 mg/dl for diabetics); GFR <10 ml/min
- Symptoms: uremia; oliguria; confusion; nausea; vomiting; pruritus; restlessness; hyperkalemia >7.0, not responsive to treatment; intractable fluid overload, not responsive to treatment

Cardiac Disease

- Symptomatic despite optimal treatment with diuretics and vasodilators
- Recurrent CHF
  - Ejection fraction <20%
- New York Heart Association Class IV
- Supporting factors
  - Arrhythmias are resistant to treatment
  - History of cardiac arrest or resuscitation
  - History of unexplained syncope
  - Cardiogenic embolic disease (e.g., CVA)

Figure 4.1. Medicare Hospice Eligibility Criteria, 2013. Guidelines adapted with permission of Care Dimensions Hospice. Figure 4.1 continues on pages 132 and 133.

Liver Disease

- PTT >5 seconds over control
- Serum Albumin <2.5 gm/dl
- End-stage liver disease
  - –Ascites refractory to treatment
  - – Spontaneous bacterial peritonitis
  - – Hepatorenal syndrome
  - – Hepatic encephalopathy, refractory to treatment
- Supportive factors
  - – Progressive malnutrition
  - – Continued alcoholism
  - – Hepatocellular carcinoma

Dementia

- Functional Assessment score = 7
  - – Unable to ambulate without assist
  - – Unable to dress or bathe without assist
  - – Urinary and fecal incontinence, intermittent or constant
  - – No consistently meaningful verbal communication
- Complications such as aspiration pneumonia, UTI, septicemia, recurrent fevers
- Decubitus ulcers stage 3 or 4
- Weight loss of >10% over last six months

Stroke and Coma

- Karnofsky Performance <40%
- Inability to maintain nutrition/hydration
  - – Weight loss >10%, serum albumin <2.5 gm/dl, pulmonary aspiration, dysphagia severe enough to threaten life
- Coma with any 3 of the following on day 3 of coma
  - – Abnormal brain stem response
  - – Absent verbal response
  - – Absent withdrawal response to pain
  - – Serum creatinine >1.5 mg/dl

ALS

- Critically impaired respiratory function
  - – Dyspnea at rest
  - – Use of accessory muscles
  - – Respiratory rate >20
  - – Reduced speech/vocal volume
  - – Unexplained headaches, anxiety, or nausea

- Severe nutritional insufficiency
  - Progressive weight loss of at least 5% of body weight, with or without gastrostomy tube insertion

HIV

- CD4 count <25 cells/mcl or persistent viral load >100,000 copies/ml
- Decreased performance status
- Supporting factors
  - Chronic persistent diarrhea
  - Persistent serum albumin <2.5
  - Concomitant substance abuse
  - Age >50
  - Advanced AIDS dementia complex
  - CHF or advanced liver disease

Figure 4.1 ends here.

Table 4.1 Levels of Clinical Care Provided by Hospice Programs

	Routine	*Continuous*	*Inpatient*	*Respite*
24-hr on call	✓	✓	✓	✓
Home health aide	≤2 hr/day			
RN visits	≤3/wk + p.r.n.			
Social worker visits	q2wk			
Chaplain visits	q2–4wk			
Volunteer	2–4 hr/wk			
MD	p.r.n.			
Occupational/physical/ respiratory therapy	p.r.n.			
Continuous nursing		≥8 hr RN/day		
Inpatient care			p.r.n.	
Respite care				5 days/month

Note: Continuous home care is for patients with, for example, refractory cough, dyspnea, pain, or delirium; they can receive 24-hour nursing and home health aide services.

Inpatient care, rarely utilized, is for refractory symptoms that cannot be controlled at home, even with continuous care. The referring physician admits the patient and may bill for services under Medicare Part B.

The goal of *respite care* (in a community skilled or intermediate nursing facility) is either to provide a rest for the caregiver or to remove the patient to an adequate facility when the home is temporarily inadequate to meet the patient's care needs.

Finally, the hospice team tries to ensure that families are comfortable with the choices they have made about the patient's care so that they will have no guilt about these choices when the patient dies. In *Dying Well,* Dr. Ira Byock shares an important technique he uses for helping families explore these issues. For example, when asking a family to consider discontinuation of tube feedings, he says to them, "This is wrenching stuff, so take as much time as you need. None of us, in the months to come, and especially after [the patient] has died, wants to look back and wonder whether we did the right thing" (1997, p. 180).

I have begun using this approach each time I ask for family input in a significant decision, such as *"Should a feeding tube be placed?"*; *"Should we change the focus to comfort care?"*; or *"Will you be able to keep him here at home when he is dying?"* I ask the family to imagine that it is now several months since the patient has died, and they are looking back at the choices I am asking them to make now: *"How do you feel about this decision? Do you still think we did the right thing? Was everything we did in agreement with* [the patient's] *values and goals, and with yours?"* If they are able to answer yes to these questions, they are much more likely to remain at peace with their decisions after their loved one dies.

Anticipating House Staff Concerns

"Don't you care at all?"

Our palliative care team had been consulting on the care of Oma, a young woman dying from a refractory metastatic gynecologic cancer. She was much loved by her house staff and the nurses on the unit, who had known her for several months. She and her family had come from the Dominican Republic to seek help for her condition, but it appeared no help was possible. The tumor had continued to grow despite everyone's best efforts. It swelled her abdomen and afflicted her with abdominal pain and finally with hypercalcemia, which, too, was refractory to medical efforts at correction.

Oma was well supported by her family and friends. Her mother had been with her throughout the months of her stay in the United States. In her last weeks of life, Oma reunited with her estranged husband. Her family was allowed to be in close attendance, and together, we were able to give her the comfort she needed, and she died peacefully under our care in the hospital.

But we did not achieve this easily, even though Oma had accepted comfort care, understanding that there was no further antineoplastic therapy to try. While the house staff and nurses shared the goals of our palliative care team, they were

often puzzled by and resisted implementing our recommendations, which included discontinuing intravenous fluids that were only exacerbating her ascites and peripheral edema, and stopping the monitoring of her electrolytes and calcium levels. The morning we made those suggestions, an angry intern asked me, "Don't you care at all?" At the time, I did not understand why she would think I didn't care about Oma. Though our approach was different from theirs, it provided the comfort they said they were seeking for her.

The answer appeared only after her death, while we were meeting with members of the gynecologic oncology team at their request. They could not understand how we and they had observed the same patient and yet found different problems that required totally different solutions. They were saddened by Oma's death and feared that they had contributed to her suffering. They wanted to understand better how to help future patients.

This was the first time they had worked with a palliative care team, and so they asked us, *"How do you know when it's time to stop what we normally do?"* How should they think about caring for someone who was on comfort care? What criteria did we use as we made our recommendations? For example, why didn't we want them to monitor her calcium and potassium levels? Why did we oppose "fluid challenges" (i.e., rapid infusions of 500-ml bolus doses of IV fluid) when she was tachycardic, up to 150/min? *"Why,"* the nurses had asked, *"do they want us to do an enema in someone only days from death?"*

It was not the details of day-to-day management that they needed to understand; they needed a new appreciation for how different the goals are when you care for dying hospitalized patients. We suggested that the gynecologic oncology team treat these patients as though they were caring for them at home, perhaps with the help of a hospice team. There, the goals and priorities of the patient and family—not the disease or metabolic abnormalities—are paramount.

We suggested that instead of weighing the risks and benefits of each intervention, they ask themselves what is the *burden* versus the *benefit* of this intervention? How will it help us further the patient's and family's goals? We acknowledged that assessing the burden/benefit ratio was very different from assessing risk/benefit, with which they were more familiar. After all, only minimal risk is entailed in a venipuncture or a fluid challenge. But there is a great deal of potential burden, especially in someone whose ascites, pulmonary secretions, and edema are going to be markedly exacerbated by the fluid.

House staff, it seems, spend much less time visiting the rooms of patients like Oma, who are receiving comfort care, than those of other patients (Mills et al. 1994). Perhaps that's because they, like Oma's team, don't know how they can help. The gynecologic oncology team was troubled about its role in providing

comfort care for Oma. This did not look like "care" to them: *"If we aren't drawing blood, or monitoring her vital signs, what should we do?"* They felt helpless and at sea; they felt they'd had no more to offer to Oma or her family.

We explained that there are many other ways to show concern. Providing excellent comfort care, for example, requires frequent observations of patients and their families and an understanding of what causes distress for dying patients. We explained that we'd asked them to stop the fluids to prevent her having breathing difficulties due to the excess hydration, and we had asked for the enema because we had surmised that obstipation due to the continuous opioid infusion and refractory hypercalcemia was causing her significant discomfort and could contribute to her risk of developing delirium. We also explained how the house staff's frequent visits to Oma and obvious concern for her had provided comfort to her family. By the end of this meeting, the team members said they had begun to understand the other ways in which they could provide care and the other goals they could to try to achieve for their dying patients.

Physician-Assisted Death

As I write this, physician-assisted death (formerly referred to as physician-assisted suicide) is legal in Oregon, Washington, and Montana. The "Death with Dignity" initiative on the Massachusetts ballot in November 2012 (which is identical to the Oregon law) was narrowly defeated. It is clear from these legal efforts that anticipating family concerns and enabling the family and the home care and inpatient teams to provide expert symptom management may not be enough to convince some patients that life is still worthwhile; they want the right to end their lives at a time of their choosing, when they are still in control.

Requests

I have been asked many times either to hasten someone's death or to assist patients who want to end their own lives. The first request I had was from an unexpected source.

The Patient Who Seeks Help in Dying

I was caring for Mr. D'Angelo, a 55-year-old man with Waldenström's macroglobulinemia. Plasmapheresis controlled his blood viscosity, but he had anemia, massive splenomegaly, and an acquired coagulation inhibitor that had caused a von Willebrand's–like disease that was refractory to clotting factor replacement.

His only symptoms were weakness and shortness of breath when the anemia became too severe. Splenectomy might have helped, but his coagulopathy made the operation impossible.

Mr. D, as he asked us to call him, was an active gardener and had often brought me homegrown vegetables and herbs. Now, however, even with transfusions, he noted he was getting weaker, and one day, even using his walker, he felt too weak to ambulate. He asked whether he would ever get out of his wheelchair again, and I told him that I didn't think he would. He replied, *"Fine, doc. Then I guess it's about time for you to help me to 'get out' permanently. Life in a wheelchair is not for me."*

I was taken aback. Other than being in a wheelchair, he did not seem to me to have a life that was not worth living. Except for his weakness, his symptoms were easily controlled, and his mind was working very well. At the time, projecting my standards of an acceptable quality of life onto Mr. D, it seemed inconceivable that someone would want to die just because he had to use a wheelchair to get around. If he had been closer to the other end of the spectrum—bedridden or in severe pain—I could have understood his request. But for Mr. D, the wheelchair created limitations that were simply not acceptable; his quality of life was unsatisfactory, and he wanted to die.

I did not act on his request, and I was unable to comfort him. He refused psychological help but said he would allow a visit from his parish priest. A week later his wife found him dead in his wheelchair. The autopsy, which she requested, revealed a massive myocardial infarction.

Causes of requests for physician-assisted death. Mr. D'Angelo was the first, but since then, like many other physicians, I have had other patients ask me to kill them or to help them end their lives. Studies indicate a number of reasons that patients make such requests.

WHY PATIENTS REQUEST PHYSICIAN-ASSISTED DEATH

- Patients lack technical expertise.
- The physician is expected to serve as "guide, companion, and caretaker."
- Patients worry about adequate symptom control now and in the future.
- Patients worry that the family will be unable to care for them.
- Patients do not wish to burden the family.
- Patients experience loss of personhood, sense of worth, and meaning in life.
- The physician's attention to the patient's concerns is felt to be inadequate.

In their 1994 paper on this subject, Block and Billings suggest that patients ask us to kill them because they expect us "to be a guide, companion, and caretaker in their final passage. Patients, in fact, lack the technical knowledge to kill themselves quickly and comfortably" (p. 2040). Since we have been managing their care throughout the treatment phase of their illness, they expect us now to provide the expertise to help them die.

Block and Billings also list a number of reasons that patients who seem to have a lot to live for, like Mr. D, want to end their lives. Some may be concerned that as they get sicker, we will not provide effective control of their symptoms. They may have had bad experiences with the health care system in the past, feel that their symptoms were inadequately treated, and fear a prolonged period of unalleviated suffering.

They may also fear that their family will fail them. The diagnosis of cancer and the side effects of the treatments may have stressed the family's emotional and financial resources already. Patients may feel their family is overwhelmed or even resentful. Patients who are well cared for may feel that in the future, they will become too great a burden. They cannot risk putting it to the test: failure would be too painful.

When I was their oncologist, I knew that they might also fear that I would abandon them. I would let my patients know almost from their first visit that I would be there "for the duration." I half-jokingly said, "*You know, once you're in my care, there's nothing you can do to get out. You can take or reject my suggestions for treatment, but you can't get rid of me. You're stuck with me until the end.*" Often just my willingness to listen and to give them the security that I would not abandon them offered enough comfort.

I am also convinced that for patients who know they are dying, there are unique opportunities for growth that they would miss if they ended their lives prematurely. In my current role as a palliative care physician, I encourage patients to search for new meaning in altered life roles, to accept borrowed strength, and to pursue transcendence (Cassell 1991). I suggest they try to replace some of the losses caused by their illness by finding new roles for themselves in their communities and within their families (Byock 1997).

In Byock's *Dying Well*, for example, Mayor Burke came to understand that by accepting help from a hospice program, his neighbors, and his family, he was filling an important community role and bringing satisfaction to a number of people. It was his final gift to them. As he said, "I guess it's time to be on the receiving end" (p. 97). The dignity that he sought lay not in his physical condition (he was dying of amyotrophic lateral sclerosis [ALS]) but in something larger, which had, if anything, grown as his health had worsened.

Finally, there are patients who simply want us to pay more attention to their concerns, and they use the request for physician-assisted suicide to shock us into doing so. While we were concentrating on their physical problems, we may have overlooked their psychological, spiritual, or even financial concerns. Requests for euthanasia or assisted death suggest that the patient harbors such worries and that they are very serious. Asking us to end their lives may be the only way patients feel they can enlist our aid in ending their suffering.

Other contributing factors include physical or psychological disorders and the patient's personal values. Patients suffering from uncontrolled pain, depression, anxiety, organic mental disorders (such as delirium or brain metastases), or personality disorders are more likely to want to die. And unfortunately, both inadequately controlled pain and psychiatric disorders are common in the terminally ill patient population. In addition, patients who are grieving the many losses associated with their illness (loss of "personhood" as well as physical, social, financial, and spiritual losses) may feel that death offers the best answer.

When you encounter patients in this kind of despair, you should, in addition to evaluating them for reversible causes, have a low threshold for referring them to professionals skilled in treating psychological, social, and spiritual problems. In most cases you or these other professionals will be able to reduce the suffering of these patients, and they will no longer want to hasten their death.

Patients' personal values also may lead to requests for euthanasia or assisted death. People for whom remaining in control is especially important may feel that relinquishing control or their independence is worse than dying. They cannot imagine becoming dependent on anyone. Patients who have always been self-reliant, who have had trouble accepting help from others, or who have never been comfortable with the disabilities of others may find it intolerable to be in such a position themselves. That is what they are asking you to prevent. In retrospect, I think Mr. D may have been such a person.

There are also narcissistic people whose view of an acceptable life is different from their physicians'. A narcissist has "a pathologic need for control, a dysfunctional sense of entitlement, a basic sense that nothing is good enough, and a profound difficulty in trusting others . . . Clinicians may perceive such patients as cold, ungrateful, demeaning, or help-rejecting . . . [Such patients] also may be relatively assertive and demanding toward health care workers, and unwilling to accept professional opinion" (Block and Billings 1994, p. 2043). Euthanasia requests from such difficult patients may be among the hardest to handle.

How to respond to such requests. Physicians' personal responses to requests to assist in a death vary widely (Block and Billings 1994). Some of us avoid the

subject and deny to ourselves that it was even raised. Others feel guilty or depressed about forcing the patient to continue an unwanted, suffering-filled existence. From time to time, a few of us, especially those of us who know the patient well, comply.

There are several ways to deal with such a request other than acceding to it (Block and Billings 1994). First, acknowledge it and encourage the patient to talk about what has prompted it. Then offer a compassionate, consistent presence to the patient and his family. Next, be clear about what you will and won't do. Although you might be willing, for example, to provide pain medicine, the patient should not expect that you will actually administer a bolus of drug intended to kill him.

Finally, address the change in your relationship with the patient that results from a request for euthanasia or assisted death. Ask how he will feel about you if you reject his request—how it will affect future requests of other kinds, and whether it diminishes his trust. Reiterate your offer of help, short of killing him, and let him know that if he now feels he needs to see another physician, you will understand.

The Debates about Legalizing Physician-Assisted Death and Euthanasia

As I prepare the third edition of this book, physicians, ethicists, lawyers, politicians, and the public are still engaged in a heated debate about the right to legal physician-assisted death on the one hand, while on the other, characterizing discussion of advance directives and goals of care at the end of life as "death panels." Issues of patient autonomy have come to the forefront, with increasing expressions of concern among our patients that we will force them to stay alive despite their wishes to the contrary. To protect themselves, many people are completing living wills and assigning powers of attorney for health care (health proxies).

Disturbingly, there is evidence from several studies that these concerns are not unfounded: we physicians do not always make it our business to know our patients' wishes about resuscitation or life-support measures. Even if patients have a living will, many doctors fail to honor their requests to withdraw or withhold life-support measures.

Withholding or withdrawing of treatment is *legal,* even if it means that the patient will die as a result. Religious leaders as well as legal experts and ethicists agree that withholding or withdrawing such therapy should be distinguished from euthanasia and from physician-assisted death. Euthanasia is currently *illegal*

in all fifty states, and in thirty-nine states (Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Virginia, Wisconsin), there are statutes that expressly forbid physician-assisted death. Three states criminalize assisted suicide through common law: Alabama, Massachusetts, West Virginia; and the District of Columbia. Nevada, North Carolina, Utah, and Wyoming have no specific laws or unclear laws in this area. Oregon, Washington, Vermont, and Montana are the only states that permit physician-assisted death for mentally competent adults suffering from a terminal illness—defined as an illness that is likely to result in death within six months. Patients must consult with two physicians and wait fifteen days between requests.

The American Cancer Society, the American College of Physicians, and many individual palliative care and pain experts (such as Dr. Kathleen Foley, professor of neurology and neurosciences and professor of clinical pharmacology at Cornell University Medical College as well as former chief of the Pain and Palliative Care Service at Memorial Sloan-Kettering Cancer Center) oppose legalizing both physician-assisted death and euthanasia. As the American Cancer Society stated in its 1995 position paper, "We believe these acts are contrary to the ethical traditions and threaten the moral integrity of health care professionals. We assert that it is the responsibility of all organizations concerned with cancer care to work to improve care at the end of life, and to undertake broad educational programs for patients, families, and health care professionals concerning care at the end of life."

Dr. Foley is also concerned that with legalization, physician-assisted death would replace other, more appropriate treatment of a patient's symptoms. She argues that the state of education of most health professionals in palliative care is woefully inadequate, as is their ability to recognize chronic pain, depression, or "existential" suffering in many of their patients (Foley 1991, 1995, 1997). Most patients do not understand that, with expert palliative care, their suffering can be relieved, no matter what its cause. Even proponents of legalization of physician-assisted death, such as Dr. Timothy Quill (1993, 2004), agree that up to 95 percent of patients should be able to die with their symptoms controlled to their satisfaction.

Several surveys of both generalists and specialists reveal that many physicians would be willing to participate in physician-assisted death or euthanasia if it were legal. Since most physicians don't know other ways to relieve suffering,

perhaps they feel that death is the only humane option. According to these surveys, hospice physicians, in contrast to physicians who knew or felt they knew little about symptom control, understood that death was not the more humane option, and they were less likely to agree to participate in assisted death or euthanasia.

It is clear that now, more than ever in the past, physician education in how to recognize and relieve suffering, enhanced provision of palliative care, and public education about the efficacy of currently available symptomatic treatments must accompany any legislation that makes assisted death more readily available. The Oregon example is one that can be followed.

Palliative care availability in Oregon is the best of all fifty states, and Oregon has by far the highest percentage of the population that is able to die at home. In the fifteen years since 1997, when the Death with Dignity Act went into effect, only 1,050 people have received lethal prescriptions, and only 673 have used them (Oregon Public Health Division 2012). The concerns that uncontrolled symptoms or fear of being a burden on families would lead people to choose assisted death were unfounded. Patients who chose to take the lethal prescription, both in Oregon and in Washington, where physician-assisted death became legal in 2009 (Loggers et al. 2013), did so for three main reasons: loss of autonomy (93.5 to 97 percent), inability to participate in activities that make life enjoyable (88.9 to 92.2 percent), and loss of dignity (75 to 77.9 percent). Ninety-seven percent of these people died at home; 97 percent were enrolled in a hospice program, and 100 percent had some form of health insurance.

While we can already achieve symptom control for 95 percent of patients, what can be done for the other 5 percent? Palliative sedation to unconsciousness is a technique that can provide comfort for all patients. It can be given in the home or in a health care facility by skilled clinicians employing appropriate medications. I review the details of the technique in Chapter 10.

Some, however, consider this technique tantamount to physician-assisted death. This remains a matter of individual conscience. Many respected physicians believe that they should have the legal option to help someone who asks for help ending his life and for whom all available expert palliative care has not led to a satisfactory quality of life. They do not disagree with Dr. Foley or the American Cancer Society about the need for better education in the provision of care. But when that care has not produced a satisfactory outcome, they do not think it morally wrong to help patients end their life, or to end it for them.

This debate, regardless of its outcome, has raised the level of public discussion about the importance of providing an acceptable quality of life for patients with advanced cancer. I am hopeful that as the availability of comprehensive palliative care for patients improves, requests for euthanasia and physician-assisted death will decrease.

Self-Care

Caring for even one patient who is dying with advanced cancer can be intellectually and emotionally exhausting. Like the families you work with, you may need to develop some self-care techniques. In the course of trying to help house officers maintain their emotional equilibrium as they work with increasingly large numbers of extremely sick patients, I needed to analyze how I managed not to burn out or develop compassion fatigue. As I thought back, I realized that my initial self-care strategy was a disaster.

The first time I recall needing a strategy for self-care was in 1971, when I was a second-year medical student taking my first clinical rotation: pediatrics. But this pediatrics was not in an outpatient office or even community hospital setting. The children I saw had been admitted to a tertiary care hospital to be treated for leukemia, which at that time was almost invariably fatal, or for illnesses of similar severity and complexity. The general pediatrics ward was filled with children with cystic fibrosis. Women were scarce in medicine back then, so I instinctively knew that crying in response to what I was dealing with was "not an option."

But a great deal of what I saw called for tears. I eventually found a place to shed them in private, when I was relaxed, and I could take my time to review the emotionally charged events. Sometimes I found myself crying silently during a concert and feeling better when the concert ended. That safety valve seemed to work so well that I used it throughout pediatrics.

But many years later, when I was in the midst of my first year of clinical training in oncology, an odd thing started to happen. I found myself dreading attending concerts. Both my husband and I had looked forward to summer evenings spent at an outdoor orchestral performance, but I began to find reasons not to go. Finally, one evening, I said, "I'm just not up to that tonight!"

My husband, quite puzzled, replied, "Up to what? Why would anyone not be 'up to' hearing Mozart?" It was only then that I realized what had happened. To deal with the troubling feelings aroused by the tragic stories of the cancer patients I was caring for, I had automatically reactivated my earlier mechanism: grieve

them in private, usually during the slow moments of symphonies. What I wasn't "up to" was a mental review of the patients I'd seen recently or the full experience of the grief I had suppressed so that I could get through the work. I had developed compassion fatigue.

Compassion Fatigue

Compassion fatigue is the detachment and depersonalization that develops in therapists who care for people who have experienced extreme suffering (e.g., torture or rape) and in clinicians like emergency department specialists, oncologists, and palliative care physicians, who are emotionally affected by the trauma their patients experience. It develops in clinicians whose patients have prolonged downhill courses, who suffer severely, and about whom clinicians feel "guilty, insecure, frustrated, or inadequate" (Meier et al. 2001; Nouwen 1972). It is no wonder, then, that medical students (Dyrbye et al. 2008), residents (Thomas 2004), intensive care staff, oncologists (Vachon 2010), and palliative care practitioners are particularly prone to developing compassion fatigue (Kearney et al. 2009).

COMPASSION FATIGUE

- Feeling "guilty, insecure, frustrated, or inadequate" when caring for patients with persistent downhill courses
- Experiencing detachment and depersonalization
- Undergoing PTSD-like manifestations: hyperarousal, reexperiencing, and avoidance
- Having stress-related medical disorders, anxiety, depression, substance abuse, and family disruption
- Avoiding timely discussion of prognosis and true burdens and benefits of therapy
- Experiencing burnout (from cumulative grief and compassion fatigue)

Those of us who develop compassion fatigue are more likely to have stress-related medical disorders, anxiety, depression, substance abuse, and family disruption (Meier et al. 2001; Shanafelt and Dyrbye 2012). Some of us begin to resemble a patient with post-traumatic stress disorder: we develop (1) hyperarousal, (2) reexperiencing, and (3) avoidance (Wright 2004). Manifestations of our

hyperarousal can be anger at our own staff, colleagues, or even patients with refractory disease or their families. Having dreams or nightmares about conversations with patients whose disease is relentlessly progressive is a clinician's way of "reexperiencing." If you know someone who is too detached or depersonalizes her patients, makes fewer or no visits to patients who are doing badly, or does rounds when they are likely to be asleep and the family not there, that's avoidance. They're doing that because it is too painful for them to be there; they may even take more and more time off work. If any of this seems familiar to you or is a pretty good description of a colleague's recent behavior, you or they may be suffering from compassion fatigue.

I believe that unrecognized compassion fatigue among oncologists inhibits the timely discussion of prognosis and of the true burdens and benefits of therapy, as well as the collaboration between oncologists and palliative care clinicians who can help share the burden of these difficult conversations. Oncologists with compassion fatigue may even recoil from reaching out to palliative care colleagues, not recognizing that they do this because of often unconscious painful memories of the many tough meetings they have had together. One oncology fellow, for example, responded to my greeting in the elevator with, "I can't talk to you now; I don't have time to cry." When I hear, "He's not ready for palliative care," I sometimes wonder, "Who isn't ready?"

Palliative care clinicians also suffer from compassion fatigue for the same reasons as oncologists do. They strive to cure suffering with the same energy and commitment as oncologists apply to curing their patients, or to prolonging their patients' lives as long as possible. Caring for a patient for whom we cannot relieve or even ameliorate suffering is therefore incredibly painful for us. Palliative care clinicians are often overworked, with little control of their schedules, and they feel a moral mandate to see all the patients who need them. In some settings, they practice alone, without the support of an effective team to help them process the emotions the work engenders. It is no surprise, then, that palliative care clinicians also develop compassion fatigue.

In both oncology and palliative care clinicians, cumulative grief and compassion fatigue lead to burnout (Shanafelt and Dyrbye 2012)—those who cannot bear to sit and talk with patients, because they see their patients' impending deaths or intense suffering and feel helpless in the face of that prospect, cannot offer the presence these patients need. Without an opportunity to express those griefs and diminish their power, the clinician has less and less "room" for emotional engagement with patients, or even with her own family. For someone suffering from compassion fatigue, even making a referral to palliative care may

open doors that the oncologist who suffers from compassion fatigue may not be emotionally ready to go through.

Solutions. Once I understood what I'd been doing, that waiting until I was at a symphony to let myself experience my grief was not a good solution, I was able to devise other strategies for dealing with my grief in a much more timely fashion. After someone died, I cried if I needed to and even found a few minutes to give full vent to my sadness. I found private places around the hospital, or confided in colleagues who then felt free to share their stories with me. These resources served me well throughout my career as an oncologist.

When I began doing full-time palliative care, I again found myself challenged by the almost incessant suffering I saw. Each of us needs to identify a way to process the intense emotions the work entails. Some meditate, others exercise, but all recognize that unless we grieve our losses, we will no longer be able to remain present in the face of suffering, or to offer compassion. We need to be attentive to our own emotional and spiritual needs.

My meditation practice improved my ability to connect with my patients and to relieve some of their distress. And thanks to the wonderful clinicians I am privileged to work with on our team, I have not succumbed again to compassion fatigue. My social work colleagues on the team have been particularly helpful, but all of us look out for each other. Our motto is "never worry alone." Most recently, our palliative care team members sought training together in mindfulness meditation, using a course adapted from the work of Jon Kabat-Zinn (Stahl and Goldstein 2010; see also Chapter 7 in this book). Self-awareness or mindfulness training have both been demonstrated to help prevent burnout (Kearney et al. 2009; Stahl and Goldstein 2010). I use the exercises I've learned to prepare for or to recover from emotionally charged situations.

Training. We teach our palliative care and oncology fellows about the importance of self-care and of recognizing the stresses that their choice of profession will entail. For them and for you, the first thing to do is to acquire the core skills of conducting difficult conversations through mentoring from palliative care clinicians or oncology communication experts. Second, identify dysfunctional beliefs: "Limitations in knowledge is a personal failing; responsibility is to be borne by physicians alone; altruistic devotion to work and denial of self is desirable; it is 'professional' to keep one's uncertainties and emotions to oneself" (Novak et al. 1997, p. 503). Third, forgive yourself, accept your limitations, and accept praise; recognize and let go of mistakes, opportunities lost or mishandled; search for sources of pain and get help to learn to live with it, or do what needs to be done to help diminish it (Novak et al. 1997). Other strategies are listed in the box below.

CLUES FOR SELF-PRESERVATION

- Recognize how stressful caring for dying patients can be.
- Give yourself credit for the work you are doing.
- Learn how to work with a team; delegate and thereby diffuse responsibilities; let other team members help you.
- Monitor your emotional reactions and take time for yourself when you need it.
- Set appropriate goals; acknowledge medicine's and your own limitations.
- Collaborate with a palliative care team.

Balint groups for palliative care and oncology fellows facilitated by skilled psychologists, palliative care clinicians, or trained oncologists can also serve as a forum for discussion and exploration of grief-inducing clinical encounters, and for normalizing these feelings. We should train the fellows in how it feels to say good-bye, and why it is important to do so, both for patients and for clinicians, as well as how useful it is to write bereavement letters and make bereavement phone calls.

Kearney (Kearney et al. 2009) also offers strategies (supported by variable strength of evidence) that can prevent or treat compassion fatigue. These include "mindfulness meditation; reflective writing; adequate supervision and mentoring; sustainable workload; promotion of feelings of choice and control; appropriate recognition and reward; supportive work community; promotion of fairness and justice in the workplace; training in communication skills; development of self-awareness skills; practice of self-care activities; continuing educational activities; participation in research; mindfulness-based stress reduction for team; meaning-centered intervention for team" (p. 1159). They also offer both self-care and self-awareness practices that can be done at work.

Rachel Naomi Remen, MD, clinical professor of family and community medicine at the University of California, San Francisco, teaches undergraduates, graduates, and practicing physicians about the emotional, psychological, and spiritual aspects of care for the dying. She notes that our problems in this area may arise from our lack of experience in recovering from our own losses. We are not often shown how to process feelings associated with loss and are encouraged to develop defenses designed to deflect them. Rarely are such shields effective; more often, we succeed only in repressing painful feelings. These feelings then become even more powerful, evading our consciousness, resisting cognitive understanding, and yet directing our behavior. Because we avoid opening a

wound of our own that we do not know how to heal, we risk becoming blind to the needs of our patients.

Dr. Remen's writings (1996), workshops, and courses at the Institute for the Study of Health and Illness (ISHI; www.ishiprograms.org) help physicians experience the consequences of losses in their own clinical practices and teach them how to heal themselves. They learn to feel the pain of past losses and to mourn them effectively. At the end of the process, they often find they have regained their equanimity and joy in being physicians. Those who have gone through such experiences are also more likely to be sensitive to the needs of their dying patients. They understand that they need not have guilt or shame contemplating their patients' deaths, and they truly understand that while they cannot always cure, they can always help.

In some cases, just collaborating with a palliative care team will make the process bearable. We can help your team conduct those tough conversations (Gilligan 2003; von Roenn and Temel 2011) and later process the grief, leaving all of you better able to support and be empathetic with your patients; more aware that the limitations are medicine's, not yours; and proud of what you can offer them.

Grief Rounds

Palliative care clinicians can also help house staff process their grief and prevent compassion fatigue. At Brigham and Women's Hospital, where we currently work, the chief medical residents asked Dr. Susan Block and I to support the house staff on the oncology and bone marrow transplant teams. Dr. Block had completed an intensive study of the reactions of house staff to the deaths of their patients, finding that members of the house staff often had unresolved feelings of grief or guilt or anger about these deaths. The attending rounds in ICUs and in oncology were not able to find room for a discussion of the events surrounding a death, for airing house staff's concerns, and for education about the grief and bereavement not only of families but also of professional caregivers, such as nurses and physicians.

We therefore began to conduct grief rounds every other week, to which the interns were invited. The discussions were confidential and, of course, food and drink were provided. The chief residents, who arranged for the food, also reminded the busy interns to come to the rounds, instructing them to sign out their beepers to their residents for the hour.

These rounds were well attended. Interns shared their concerns, learned that many of their colleagues had the same concerns, and worked out ways to interact more comfortably with patients who are dying and with their families. Grief rounds were discontinued some years ago, but in 2013 the oncology fellowship

director asked our palliative care team to host weekly rounds with the physician assistants, medical students, and house staff on the oncology and transplant teams. We are finding that these weekly palliative care rounds provide another forum for discussing troubling issues when they arise. I am hopeful that the rounds will prevent these young clinicians from developing the kind of dysfunctional mechanism I had used to protect myself from the grief I was feeling.

Summary

Communication among patients, families, and clinicians is crucial as patients approach the end of life. By avoiding misunderstandings about the goals of therapy; by clarifying patients', families', and clinicians' priorities; and by reinstating patients' personal calendars, clinicians can help patients and their families make the transition to comfort care. Readdressing the issues of resuscitation and reviewing the concerns of dying parents who have young children, of family elders, and of families and patients who are waiting for a miracle can help them make truly informed choices. Understanding a patient's request for aid in hastening death, and acknowledging the effect those requests have on us, can help us stay connected and useful to patients and their families. If their goals change to comfort care, hospice programs can help alleviate family insecurities.

Along with our patients, our house staff and oncology fellows are equally in need of our support and education. We can provide these by answering their question, *"How do we know when it's time to stop what we normally do?"*; we can offer strategies to prevent compassion fatigue, and a forum such as grief rounds or palliative care rounds, where they can share difficult experiences and gain skills in challenging communication tasks. With the help of the hospice team (for patients at home or in a long-term care facility) and the palliative care team, clinicians can provide comprehensive assessment and sophisticated management of patients' concerns; patients and families can be helped to reach their final goals; and requests for physician-assisted death can be minimized. Using self-care techniques to renew and reenergize themselves, clinicians can continue to accompany their patients during their last journey.

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CHAPTER 5

Assessing the Patient in Pain

Types of Cancer Patients with Pain
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    Audit-C and Opioid Risk Tools
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Reevaluate When the Pain Pattern Changes
Summary
Bibliography

Why an entire chapter devoted to assessing pain in cancer patients? Pain, after all, is something physicians already know a lot about. It is one of the most common complaints for which patients seek their help, and physicians routinely elicit comprehensive descriptions of the pain to aid them in diagnosis. But with all the advances in pain therapy, as recently as 2008, patients still reported that their pain was not adequately treated. In the largest prospective study to date of pain in outpatients with cancer, more than 3,000 outpatients with breast, lung, colorectal, or prostate cancer were enrolled, and the findings, published in 2012,

were disturbing (Fisch et al. 2012). Of the more than 2,000 patients who told the investigators that they were having pain, 670 patients (34 percent) were not getting adequate pain medication. Twenty-three percent of patients with severe pain and 27 percent of those with moderate pain were getting no analgesic at all, and only 40 percent of patients with severe pain and 27 percent of patients with moderate pain were treated with a strong opioid. The odds of a minority patient having inadequately treated pain were twice those of a non-Hispanic white patient; not being on active treatment, having a good performance status, and being treated at a site where the majority of patients were minority all predicted inadequate pain management. This cultural disparity is unsettling and suggests a lack of belief of the patient's complaints of pain, which I discuss later in this chapter.

To treat any cancer patient with pain, clinicians need to be able to assess all the causes. In cancer patients, the cancer or its treatment is overwhelmingly likely to be the problem. Only about 5 to 10 percent of pain in cancer patients is caused by diseases common in patients who don't have cancer. Ninety to 95 percent of cancer pain is due to the cancer, resulting either directly from tumor involvement (about 75 percent) or from treatments for the disease (about 15 to 20 percent), such as mucositis caused by chemotherapy or radiation therapy. The procedures needed to stage the cancer also cause significant distress. Pain was reported by almost 70 percent of patients undergoing bone marrow aspirate or biopsy, 14 percent undergoing lumbar puncture, and 10 percent having catheters placed (Portnow et al. 2003). In 25 percent the pain was moderate, and in 25 percent it was severe. Oncology patients' pain is frequently exacerbated by the psychological, social, and spiritual stresses of their disease.

In addition, a number of pain syndromes are typically seen in cancer patients. Mr. Young, for example, a patient with lung cancer whom I took care of when I still practiced oncology, had a referred pain syndrome peculiar to patients with cancer. About three months after completing radiation therapy to his lung lesion, he developed severe right hip pain. Findings from x-rays of his hip and pelvis were entirely normal, and the bone scan confirmed the absence of metastases in this region. But the scan did reveal a metastasis in his thoracic spine, at T12. After radiation therapy to this lesion, the referred hip pain entirely resolved.

For all these reasons, the complex pain problems of many cancer patients are difficult to evaluate. Inasmuch as an accurate pain assessment is the key to effective therapy, this chapter delineates the elements of a comprehensive pain assessment in cancer patients.

Types of Cancer Patients with Pain

Cancer patients who develop pain vary in their personalities and past experiences, as well as in the nature of their disease, its stage, and where they are in their course of treatment. Pain assessments should take into account not only the stage of the disease but also the current pain syndrome and any past history of pain or substance abuse (Abernathy and Foley 2011). Patients with acute cancer-related pain, for example, usually tolerate their pain well psychologically. They know that the pain is likely to respond to antineoplastic therapy or, for those with treatment-related complications, likely to resolve entirely with time.

Patients with chronic cancer-associated pain (lasting more than three months) have "meaningless" pain: the pain does not alert the patient to something that can be fixed. Therefore, the assessment of the psychological, social, and spiritual responses of the patient to this "meaningless pain" must be very extensive. I discuss these evaluations in more detail later in the chapter. Since the source of the pain in these patients can rarely be eliminated, treatment is usually focused on maximizing function and minimizing symptoms.

Two groups of patients—those with a history of nonmalignant chronic pain who now have, in addition, chronic cancer pain, and those with a history of drug dependence—require special management techniques, discussed in Chapter 6. Finally, for dying patients, for whom the sole goal is to maintain comfort, we must address all causes of suffering related to dying, including the psychological and the spiritual.

Guidelines for Assessment of Cancer Pain

Clinical Guidelines

Experts with years of experience in pain research and in consultation and treatment of patients with pain emphasize the importance of a thorough pain assessment. Most mistakes in diagnosing the cause of a pain syndrome and failure to manage the problem effectively stem from neglecting one or more components of the following assessments:

Clinical Guidelines for Assessment of Pain

1. Believe the patient's complaint of pain.
2. Take a careful history of the pain complaint to place it temporally in the patient's cancer history.

3. Assess the characteristics of each pain, including its site, its pattern of referral, and its aggravating and relieving factors.
4. Clarify the temporal aspects of the pain: acute, subacute, chronic, episodic, intermittent, breakthrough, or incident.
5. List and prioritize each pain complaint.
6. Evaluate the response to previous and current analgesic therapies.
7. Evaluate the psychological state of the patient.
8. Use validated tools to determine whether the patient or the patient's family has a past history of alcohol or drug dependence.
9. Perform a careful medical and neurological examination.
10. Order and personally review the appropriate diagnostic procedures.
11. Treat the patient's pain to facilitate the necessary workup.
12. Design the diagnostic and therapeutic approach to suit the individual.
13. Provide continuity of care from evaluation to treatment, to ensure patient compliance and to reduce patient anxiety.
14. Reassess the patient's response to pain therapy.
15. Discuss advance directives with the patient and the family.*

Risk of Aberrant Opioid Use

In 2013, death from prescription drug abuse has become a more common cause of death in the United States than abuse of illegal drugs. Patients' families and friends may be at risk if they use the opioids we prescribe to manage our patients' pain, or the patients themselves may be at risk if they misunderstand our instructions about use of sustained-release oral or transdermal opioids or methadone. In response to these concerns, the FDA mandated education for prescribers of opioids, to mitigate the risk through its Risk Evaluation and Mitigation Strategy (REMS) programs. Opioids are only one of the classes of agents requiring REMS. Many chemotherapy (e.g., lenalidomide) and supportive care agents (e.g., darbopoietin alpha) also require completion of a REMS program. Pharmaceutical companies, state medical societies, and national professional societies such as the American Academy of Hospice and Palliative Medicine and the National Comprehensive Cancer Network (NCCN) (http://www.NCCN.org/rems) now offer REMS programs for physicians. The NCCN site lists all the oncology-related agents that require REMS.

*From N. I. Cherny, Pain assessment and cancer pain syndromes, in *Oxford Textbook of Palliative Medicine,* 4th ed, G. Hank, N. I. Cherny, N. A. Christakis, et al. (eds), Oxford: Oxford University Press, 2010.

The opioid REMS programs include basic information on the difficulty of determining which patients are at risk for opioid abuse; the rationale for using "universal precautions" when considering prescribing these agents to any patient; how to use a risk tool, such as the Opioid Risk Tool (described below); educating patients about the safe use and proper disposal of the various forms of sustained-release oral and transdermal opioids; providing written informed consent to everyone using sustained-release opioids, including the benefits, risks, and adverse events expected; appropriate use of random urine toxicology screens and how to interpret the results; and what elements need to be documented in a pain assessment and management program. The courses are available online, and there is an iPhone app for easy reference, "Safe Opioids," created by the Prescribers Clinical Support System for Opioid Therapy (PCSS-O). It can be downloaded for free at www.pcss-o.org/pcss-o-iphone-app-safe-opioid-prescribing.

Audit-C and Opioid Risk Tools

Assessing patients' current and past use of alcohol, and their personal and family history of opioid use or aberrant use, will help you assess the risk that the patient will use the opioids you prescribe for their pain for other purposes, most commonly to "chemically cope" with the anxiety that could better be addressed with more effective measures. There are several validated tools you could use for this purpose. Our team has chosen the Audit-C (Figure 3.2) (Frank et al. 2008) to assess for alcohol abuse, and the Opioid Risk Tool (Figure 3.3) (Webster and Webster 2005) to assess the risk of aberrant use of opioids. These are practical tools that take no more than five minutes to complete. When we identify someone at moderate or high risk, we explain our concern to the patient, alert the patient's oncology team, and urge the oncologist to add an expert substance abuse clinician (psychiatrist, psychologist, or social worker) to the treatment team as a condition of ongoing care for the patient.

AHCPR Guidelines

The pain assessment recommendations in the Agency for Health Care Policy and Research (AHCPR) guidelines, *Management of Cancer Pain,* incorporate those listed above, but they are stated slightly differently. The guidelines produced by the American Pain Society (Miaskowski et al. 2005) embody the same principles. The six AHCPR recommendations for pain assessment are:

1. Health professionals should ask about pain, and the patient's self-report should be the primary source of assessment.
2. Clinicians should assess pain with easily administered rating scales and should document the efficacy of pain relief at regular intervals after starting or changing treatment. Documentation forms should be readily accessible to all clinicians involved in the patient's care.
3. Clinicians should teach patients and their families to use assessment tools in their homes in order to promote continuity of effective pain management across all settings.
4. The initial evaluation of the pain should include:
   - a detailed history, including an assessment of pain intensity and characteristics
   - a physical examination
   - a psychosocial assessment
   - a diagnostic evaluation of signs and symptoms associated with common cancer pain syndromes
5. Clinicians should be aware of common pain syndromes: this prompt recognition may hasten therapy and minimize the morbidity of unrelieved pain.
6. Changes in pain patterns or the development of new pain should trigger a diagnostic evaluation and modification of the treatment plan.*

The remainder of this chapter considers each of these recommendations in more detail.

Ask about the Pain

Strangely enough, cancer patients, especially those with chronic pain, seldom complain about their pain during routine office visits. Often, they assume that pain is an inevitable, irreversible part of having cancer, and they see no reason to waste the time with you talking about something they don't think can be changed. Instead, they ask you about the progress of their disease, their prognosis, medication side effects, or how to reverse their increasing debility. Some may fear that you will think less of them if they are unable to deal with their pain, so they do not reveal it even if you ask how they are feeling; instead, they limit them-

*From A. Jacox, D. B. Carr, R. Payne, et al., *Management of Cancer Pain: Clinical Practice Guideline No. 9,* AHCPR publication 94-0592, Rockville, Md.: Agency for Health Care and Policy Research, U.S. Department of Health and Human Services, Public Health Service, 1994.

selves to telling the assistant who asks for a pain number as part of their vital signs, or the nurse in the infusion suite.

It is left to you, then, to ask patients directly whether they are having pain, especially if they have lesions that are likely to cause discomfort. You may need to teach them that you don't consider it shameful to have pain, any more than it is shameful to have a cough or a broken arm. By carefully questioning them and being attentive to their responses, you can demonstrate that you consider pain to be a legitimate complaint. And by managing their complaints successfully, you can correct their misconception that pain is a necessary part of the cancer process.

Believe the Patient

Cancer patients may also be reluctant to report their pain to you because they have had prior experiences in emergency rooms or other health care settings that lead them to think that you won't believe them. They may be reluctant to admit that they need a stronger opioid to relieve their pain, because in the past, especially before their cancers were diagnosed, they were treated as if they were drug addicts. We must believe the patient's complaint of pain, however, because doing so is crucial to an accurate pain assessment.

But this is not as easy as it may seem. Some people, albeit unconsciously, use cultural stereotypes that affect how they interpret someone else's pain complaint. They may think, for example, that patients from Jewish or Italian backgrounds are more likely to exaggerate the pain they are feeling than are the more stoic Scots or Swedes. One study showed that adequate pain medication was more often prescribed to nonminority than to minority patients, but the authors stated that their study did not take into account reluctance of patients or their families to report pain, take the opioid prescribed, or pay for it (Cleeland et al. 1997). Numerous other studies were similarly not controlled for important variables that affect patients' pain complaints. The few studies that have had proper controls have not shown cultural differences in pain threshold, pain expression, or coping ability. (Other ways in which culture influences pain assessment are discussed later in the chapter.)

In addition, whether or not a patient "looks" as if he is in pain may affect whether you believe his complaint. For example, you are likely to believe complaints of pain from a patient with a broken arm, because people with *acute* pain look as if they're in pain: they appear uncomfortable and anxious and are often sweating. People with acute pain look this way because their activated sympathetic nervous system causes sweating and an increase in pulse and

blood pressure. When we observe these findings, we usually believe complaints of pain.

But what about patients with *chronic* pain who do not "look" as if they are in pain? Their complaints often seem out of proportion to the amount of disease that can be documented by physical exam or x-rays. Consider the patient with severe arthritis or advanced osteoporosis with compression fractures. Her pulse and blood pressure are normal; she's not particularly anxious, and she's not sweating. Don't you find it a little harder to believe that she is in severe pain?

And don't you find it harder to treat her with opioids? After all, as I discussed in Chapter 2, many of us find it difficult to prescribe opioids when we are not sure someone is having pain, because we suspect she is using our prescriptions to "get high." Given this suspicion, we want to be confident that someone is really experiencing pain before we prescribe an opioid.

We don't have resistance like this to prescribing most other drugs, and so we don't have to be quite as sure of the diagnosis before prescribing them. If, for example, you see someone who has orthopnea and paroxysmal nocturnal dyspnea but whose physical and x-ray findings don't fully substantiate a diagnosis of congestive heart failure, you have no problem prescribing appropriate medications and monitoring the patient's response. If his symptoms improve, great! If not, you simply pursue other diagnostic possibilities.

But even if the osteoporotic patient has equally compelling pain symptoms, if you think the objective findings don't substantiate her complaint, you might well be reluctant to treat her empirically with opioids. But what are the objective findings for someone with chronic pain? What should you be looking for to substantiate her pain complaint, or the complaint of an oncology patient with chronic, severe pain? Being familiar with the presentation of patients in severe *chronic* pain makes it easier for us to decide how to treat the patient.

Neuropathic Pain

It was hard for Mr. Cirelli's physicians to believe he was in pain, though that was what led him to see his doctor. Mr. Cirelli was thought to have a Pancoast tumor, a lung cancer that, because of its location in the lung apex, often infiltrates the chest wall and the nerves of the brachial plexus. I met him while I was working at the Philadelphia VA in hematology and oncology. When the admitting resident called to ask me to see him, she apologized that no pathologic diagnosis had yet been made: *"His chest film shows a mass in the right lung apex, but I really haven't been able to do a thorough exam or obtain any tissue because Mr. Cirelli won't cooperate."* When I went to his ward, his nurses confirmed the resident's impression,

adding that Mr. Cirelli was short-tempered and demanding, and that I was unlikely to get much conversation from him.

On entering his room, what I saw was a man lying very quietly in bed staring at the TV mounted on the wall. In answer to my greeting, he slowly turned his head toward me, but the rest of his body stayed very still. He looked exhausted, but he was not grimacing or wincing. He kept his right elbow bent with his right forearm across his chest, supported by his left hand.

In response to my questions, he said that he had been well until four months earlier, when he had noticed a mild aching pain in his right shoulder area. The discomfort had progressed, and when he developed weakness in his right hand grip, he saw an orthopedist, who treated him for an injured rotator cuff. When the pain worsened and a shoulder film suggested a mass in the apex of the lung, he was referred for further evaluation. He now described the pain as excruciating (the choices I gave him were mild, moderate, severe, or excruciating). It was constant, deep, and aching, and it occasionally "shot down" his arm like electricity.

He could not move his right arm without pain and could no longer sleep except for catnaps. He had lost his appetite and ability to concentrate. The pain was his central concern. He told me all this calmly but with a very depressed affect. His pulse and blood pressure were normal, and he was not sweating. I tried to examine his right shoulder area, but he could not tolerate any evaluation of his neck, right supraclavicular area, right shoulder, or right axilla, and he would not sit up for a lung examination. His right hand showed muscle atrophy typical of the C7-T1 distribution.

Mr. Cirelli's symptoms and signs were typical of someone with chronic severe neuropathic pain arising from tumor infiltration into the nerves of his right lower brachial plexus. His physicians and nurses were not familiar with the exquisite sensitivity to touch caused by this kind of nerve injury and so could not have known how agonizing any examination of the shoulder area was for him. Since he didn't resemble patients with acute pain, they mistook his distress for obstreperousness.

Patients like Mr. Cirelli who have severe chronic pain do not sweat or have tachycardia or hypertension, but they usually guard the part that hurts and often have a generalized lack of spontaneous movement. They may appear anxious or depressed, withdrawn or angry, and may have difficulty relating to others, sleeping, concentrating, or eating.

Since I frequently cared for patients who had chronic neuropathic pain, I was able to believe Mr. Cirelli. I pointed out my findings to his physicians and nurses, then suggested that his personality might be very different if he had less severe pain. They were still skeptical but concurred that we would not be able to make a

diagnosis unless we relieved his pain. At my recommendation, they agreed to a trial of high-dose dexamethasone, which is often effective for neuropathic pain, and opioids.

Within 48 hours Mr. Cirelli was a different person. His pain was now only moderate, which was acceptable to him. He showed me how he could now move his right arm with tolerable discomfort. He readily agreed to a physical examination and to the scans and biopsy necessary to make a diagnosis. The nurses remarked on how affable and talkative he was and how helpful he had been to other patients on the ward. He was able to sleep through the night, eat, and interact with others. The relief of his chronic pain had been dramatic, and according to his family, he had become himself again.

Mr. Cirelli's neuropathic pain was a clue to his underlying pathology. Had it been recognized sooner, he would have suffered less, his lung cancer may have been discovered sooner, and his hand strength might have been preserved. When sought for, the signs of chronic pain are often apparent in various cancer patients whose complaints might otherwise seem unfounded. The signs may also be recognized in patients with intense pain of nonmalignant origin, such as chronic arthritis, diabetic neuropathy, or post-herpetic neuralgia.

Measure the Pain and the Distress It Causes

The AHCPR guidelines stress that "the patient's self-report should be the primary source of assessment." In this respect, pain is unique. We do ask a diabetic patient about his symptoms, but physicians usually rely on the blood glucose and ketone levels to adjust insulin doses. To determine the effectiveness of a pain-relief regimen, we must rely on the patient to *tell us* how his pain has changed after therapy. No one but the patient can accurately report his pain—not the nurses caring for him, not his family, not his friends. No matter how well trained we are or how well we know our patients, numerous studies have shown that all of us significantly underestimate the intensity of patients' pain.

Of course, people differ in how they experience pain. If you ask five people with broken arms to rate how much pain they are having, you are likely to get five different answers. But if you give them nothing to relieve their pain and ask them to rate it again sometime later, each patient is extremely likely to give you exactly the same rating as the first time. Numerous studies have shown, in fact, that a patient's reports of pain are consistent, reproducible, and reliable. Pain ratings after treatment are just as accurate and are used to indicate the effectiveness of a specific treatment for that patient.

Pain rating scales are subjective, not objective. But they are still *accurate*, and they provide a *number* that represents the intensity of a patient's pain. Just as doctors and nurses use blood glucose levels to gauge a patient's response to insulin, they can judge a patient's response to pain therapy by noting how the pain intensity number changes. (I describe several types of rating scales below.)

Equally importantly, physicians and nurses can ask patients whether the degree of pain relief *is satisfactory to them*. For some patients, a pain rating of 6 on a scale from 0 (no pain) to 10 (the worst pain you can imagine) is fine. These patients can tolerate the pain better than they can the side effects caused by higher doses of analgesic. For others, a level of 2 or 3 must be achieved. Mr. Cirelli, for example, told me he had "no pain" after he began taking the dexamethasone and opioids. When I pressed him for a number, he said it was a 2 or a 3. In my experience, he is typical of patients with well-controlled chronic pain, for whom "no pain" is a level 2 or 3.

I often find it necessary to explain these concepts to those I work with so that they can help me relieve a patient's pain as quickly as possible. Since pain has become "the fifth vital sign," and is measured at least every time the other vital signs are measured, most nurses and house staff are familiar with the importance of measuring pain and do it routinely. Some even do it before and after they give a patient a medication for pain, entering both values in the electronic medical record. Those longitudinal records are very helpful in guiding pain management. If, however, you find that staff is not reporting the numbers to you as you attempt to regulate the pain regimen, you might find a diabetes analogy helpful. You might say something like,

If you were taking care of someone with diabetes, you wouldn't call me and say, "The patient's blood glucose was bad, *so I gave him some insulin and it got a little* better." *I would have no idea how effective the insulin was or what the next dose of insulin should be. Well, I won't know what to do if you tell me, "The patient's pain was* bad, *so I gave him an oxycodone and now it's* better."

You're already asking the patient to tell you how severe his pain is. I'd really appreciate it if you included that information in your report to me: "The patient said his pain was a 9 out of 10. I gave him 10 mg of oxycodone, and an hour later he said his pain level was a 7 and that he was not satisfied with that degree of pain relief." That would give me all the information I needed: the 10 mg of oxycodone were inadequate, and stronger medication will be required.

I also encourage house staff to include a quantitative pain assessment in the daily progress notes of all patients with a significant complaint of pain, just as they would include the blood glucose level in the progress notes of a patient with diabetes. Since the Joint Commission on Accreditation of Healthcare Organizations

(JCAHO) has mandated the documentation of the level of pain and pain relief, many hospitals have modified their TPR (temperature, pulse, and respiration) sheets to include a continuous record of patients' pain level and whether the degree of pain relief is satisfactory to them (Figure 5.1). Studies have shown that as a result, pain control and patient satisfaction significantly increased.

TEMPERATURE

Month-Day-Year																																					
Post Adm/Post-Op																																					
Hours of Day	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	4	8	12	
160 150 140 130 120 110 100 90 80 70 60 50 40 — RECTAL • ORAL ∘ TYMPANIC × — 41 40 39 38 37 36 35																																					
Respiration																																					
Pain Intensity 10 5 0																																					
Relief Acceptable (Y/N)																																					
Weight																																					
	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	
Blood Pressure																																					
INTAKE Oral																																					
INTAKE Tube Feeding																																					
INTAKE Supplements																																					
INTAKE Intravenous																																					
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INTAKE TPN/PPN/Lipids																																					
INTAKE 8 Hour Total																																					
24 Hour Total																																					
OUTPUT Urine																																					
OUTPUT Emesis/NG																																					
OUTPUT Stool																																					
OUTPUT																																					
OUTPUT																																					
OUTPUT																																					
OUTPUT 8 Hour Total																																					
24 Hour Total																																					

Figure 5.1. Memorial Sloan-Kettering Vital Sign Sheet incorporating a Pain Documentation Form. From M. Bookbinder, M. Kiss, N. Coyle, et al., Improving pain management practices, in *Cancer Pain Management*, 2nd ed., edited by D. B. McGuire, C. H. Yarbo, and B. R. Ferrell, Sudbury, Mass.: Jones and Bartlett, 1995; reprinted with permission.

The word scales and numerical scales used in the examples above are only two of several tools that patients can use to measure their pain. These tools have been extensively tested in research settings and found to be valid and reliable; they are easy to administer and to understand. They are designed to be used by patients, their families, their physicians, and other health professionals. If you offer various types of scales and tools, patients and their families can choose one that makes the most sense to them and then learn from someone in your office exactly how to use it.

Intensity Scales

Visual Analog Scale. A Visual Analog Scale (VAS) is a 10-cm horizontal or vertical unruled line anchored at its ends by numbers or words describing the two extremes of a symptom. In the case of pain, for example, one end is labeled "0," or "no pain," and the other end "10," or "worst possible pain" (Figure 5.2a).

But patients with cancer often have more than one pain. Although the pains might be equally intense, one may be more *distressing* than another. For example, neuropathic pain, such as Mr. Cirelli's, is usually more distressing than visceral pain, such as that caused by an enlarged liver. To unravel complex pain syndromes, it is useful to determine not only the intensity of various pains but the associated distress. A VAS can also be used here; the ends would be labeled "no distress" and "unbearable distress" (Figure 5.2b).

Patients usually need instruction in using a VAS for the first time. After explaining the meaning of the two ends of the scale, the clinician asks the patient to make a mark on the line that reflects his present pain intensity, then to use a ruler to measure how far this mark is from the "no pain" end of the scale. This distance is the *pain intensity rating*. The process can be repeated to determine the average, worst, and mildest pain intensity over the preceding few weeks and to measure the effectiveness of drugs and of nonpharmacologic therapies.

For example, a patient with breast cancer metastatic to her bones who is taking only acetaminophen might have largely uncontrolled pain. She would indicate this on a VAS by making a mark close to the "worst possible pain" end of the scale. If the mark were 8.5 cm from the "no pain" end, her pain intensity would be 8.5. An hour or so after taking two 500 mg doses of acetaminophen with 10 mg of oxycodone, the patient would make a new mark to represent how much pain she was having, then remeasure. The distance might now be 4 cm, and her pain intensity would be 4. The drop from 8.5 to 4 indicates that the pills have been quite effective.

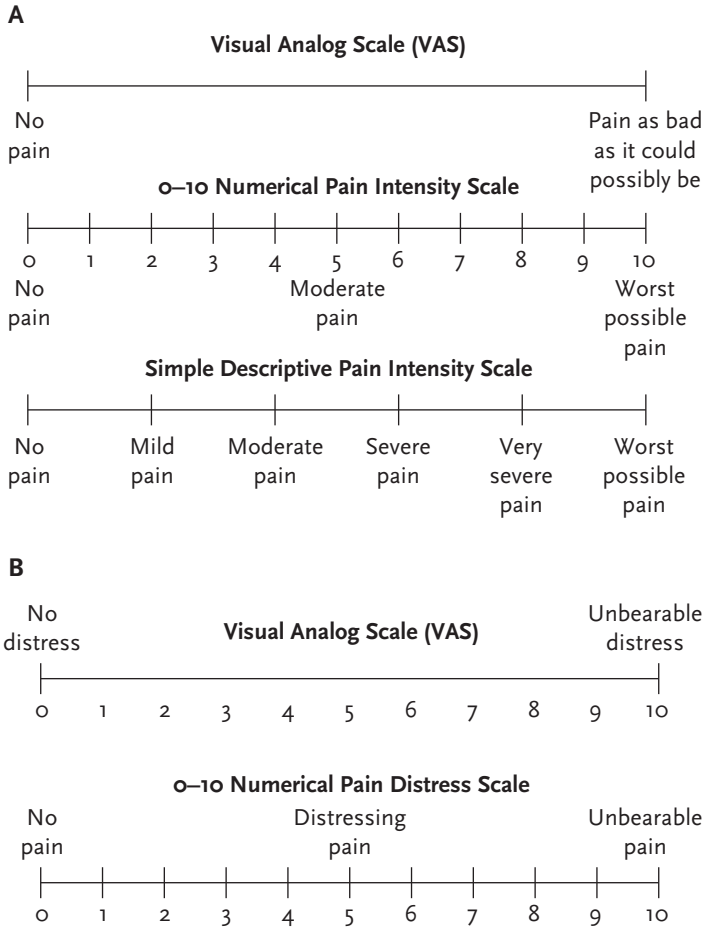


Figure 5.2. (a) Pain Intensity Scales and (b) Pain Distress Scales. A 10-cm baseline is recommended for VAS scales and for numerical and descriptive scales used as graphic rating scales. From the Acute Pain Management Guideline Panel, Agency for Health Care Policy and Research, Rockville, Md., 1992 and 1994.

If you feel that a patient will not be able to do these measurements easily, choose a scale that is already ruled in 1-cm increments, with each mark numbered (0, 1, 2, etc., as shown in Figure 5.2a and b). This ruled scale is not quite as accurate as the unruled one, because patients tend to choose a whole number rather than a fraction of one, but it is adequate for clinical purposes and is very reliable.

Most patients have no difficulty using a VAS. The scales are nonintrusive, and patients understand the concepts of assigning a number to reflect the intensity of their pain and using the scales to help them communicate how effective

the pain therapy has been. A disadvantage sometimes noted for these scales is that they rate only the intensity of the pain, not its quality or the degree of functional or psychological and social disability it induces. And some people cannot understand the abstract concept that a larger or smaller number reflects increasing or decreasing pain. These patients always assign the same number even though they clearly are experiencing varying pain intensities. You can more profitably use a functional tool, such as the Wisconsin Brief Pain Inventory described below, to assess the effect of therapy for patients like this.

Pain Assessment in Advanced Dementia and Pain Assessment Checklist for Seniors with Limited Ability to Communicate. It can be challenging to assess pain in a patient who has dementia as well as cancer. Several scales have been validated in this population. A consensus recommendation from an expert panel endorsed the Pain Assessment in Advanced Dementia (PAINAD) scale (Figure 5.3) (Warden et al. 2003) and the Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) (Herr et al. 2010). I find the PAINAD easy to use clinically. The dimensions that you are asked to observe include breathing, negative vocalization, facial expression, body language, and consolability. Patients can be scored up to 2 points in any area, and the total number of points (0 to 10) puts them in the same categories—none (0), mild (1–3), moderate (4–6), or severe (7–10)—as with the other numerical scales. Many other tools are available, some of which are validated (Herr 2011).

Word scales. For some people, it is simpler and more intuitive to rate their pain or distress on a scale that uses words instead of numbers. Word scales (descriptive scales) have been found particularly useful for patients over 70. Instead of asking them to make a mark on a line or assign a number to quantitate the pain, ask them whether they have *no pain* or pain that is *mild*, *moderate*, *severe*, *very severe*, or *worst possible*. This scale is called a Simple Descriptive Pain Intensity Scale (Figure 5.2a). Another word scale gives patients the choice of *none*, *mild*, *moderate*, *severe*, or *excruciating* to describe their pain.

There is also a word scale for the distress caused by the pain. The patient chooses a word to indicate whether her distress level is *none*, *annoying*, *uncomfortable*, *dreadful*, *horrible*, or *agonizing*. These words have been extensively tested for their ability to discriminate among different degrees of pain intensity; to maintain the reliability of the scale, these specific words must be used.

Just as with the number scales, physicians can use any of these word scales to get an idea of the range of pain and its associated distress patients have experienced throughout the day. Patients simply select which word best describes the most severe and which describes the mildest pain they have had that day.

Pain Assessment in Advanced Dementia Scale (PAINAD)

Instructions: Observe the patient for five minutes before scoring his or her behaviors. Score the behaviors according to the following chart. Definitions of each item are available in Warden et al. 2003. The patient can be observed under different conditions (e.g., at rest, during a pleasant activity, during caregiving, after the administration of pain medication).

Behavior	0	1	2	Score
Breathing independent of vocalization	• Normal	• Occasional labored breathing • Short period of hyperventilation	• Noisy labored breathing • Long period of hyperventilation • Cheyne-Stokes respirations	
Negative vocalization	• None	• Occasional moan or groan • Low-level speech with a negative or disapproving quality	• Repeated troubled calling out • Loud moaning or groaning • Crying	
Facial expression	• Smiling or inexpressive	• Sad • Frightened • Frown	• Facial grimacing	
Body language	• Relaxed	• Tense • Distressed pacing • Fidgeting	• Rigid • Fists clenched • Knees pulled up • Pulling or pushing away • Striking out	
Consolability	• No need to console	• Distracted or reassured by voice or touch	• Unable to console, distract, or reassure	
Total Score Maximum 10				

Scoring: A possible interpretation of the scores: Mild pain 1–3; Moderate pain 4–6; Severe pain 7–10

Figure 5.3. Pain Assessment in Advanced Dementia (PAINAD) Scale. Adapted from V. Warden, A. C. Hurley, and L. Volicer, Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) scale, *J Am Med Dir Assoc* 4:9–15, 2003.

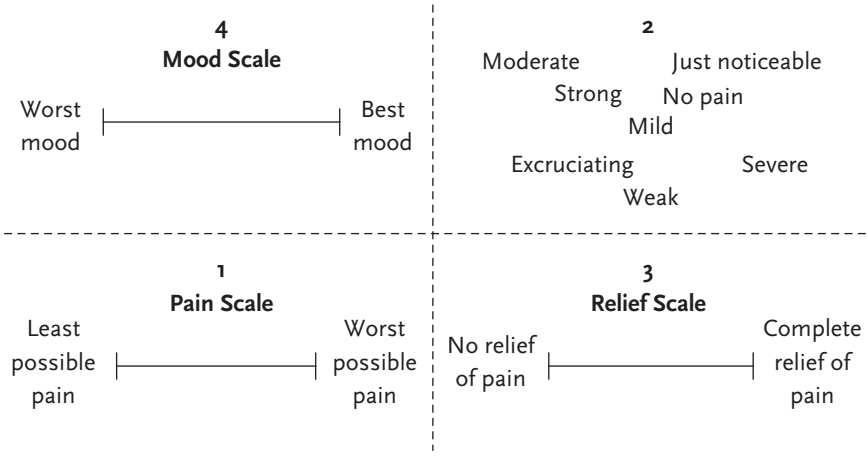


Figure 5.4. Memorial Sloan-Kettering Pain Assessment Card. The card is folded along the dotted lines so that each measure is presented to the patient separately in the numbered order. From B. Fishman, S. Pasternak, S. L. Wallenstein, R. W. Houde, F. C. Holland, and K. M. Foley, The Memorial Pain Assessment Card: a valid instrument for the evaluation of cancer pain, *Cancer,* 60:1151–1158, 1987; copyright © 1987 American Cancer Society; with permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

Pain Assessment Forms

A minority of patients cannot use numbers or words to quantify their pain, the distress it is causing, or the efficacy of therapy. For them, I rely on comprehensive assessment forms (or tools) that include a measure not only of pain intensity but also of other functional dimensions that reflect the effects of the pain on the patient's day-to-day life. These tools are also easy to use and take no more than five to ten minutes to complete.

Memorial Pain Assessment Card. The Memorial Pain Assessment Card (MPAC) (Figure 5.4) was originally developed by the Analgesic Studies Section of Memorial Sloan-Kettering Cancer Center to evaluate the relative potencies of new drugs. It was found, however, to correlate well with other validated measures of pain and psychological distress that take much longer to complete. It's portable—it fits in a coat or jacket pocket—and, when folded to allow each scale to be shown to the patient separately, allows measurement not only of pain *intensity* but also of pain *quality,* pain *relief,* and patient *mood.*

Wisconsin Brief Pain Inventory. One of the most widely used forms, which is extremely useful in unraveling and managing complicated pain problems, is the tool developed by the Pain Research Group at the University of Wisconsin–Madison Medical School (Figure 5.5). This Brief Pain Inventory, which can be

Brief Pain Inventory (Short Form)

Date _____/_____/_____ Time _____

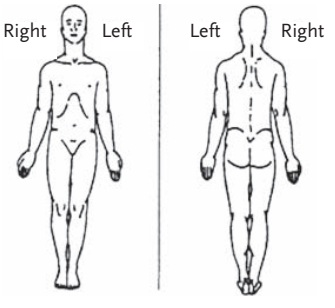
Name _____ _____ _____

Last First Middle Initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

   1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its **worst** in the last 24 hours.

   0 1 2 3 4 5 6 7 8 9 10

   No pain — Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain at its **least** in the last 24 hours.

   0 1 2 3 4 5 6 7 8 9 10

   No pain — Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the **average**.

   0 1 2 3 4 5 6 7 8 9 10

   No pain — Pain as bad as you can imagine

6. Please rate your pain by circling the one number that best describes how much pain you have **right now**.

   0 1 2 3 4 5 6 7 8 9 10

   No pain — Pain as bad as you can imagine

_____

Figure 5.5. Wisconsin Brief Pain Inventory. From the University of Texas M. D. Anderson Cancer Center; reprinted with permission.

7. What treatments or medications are you receiving for your pain?

_____

_____

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much **relief** you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
No Relief										Complete Relief

9. Circle the one number that best describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

B. Mood

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

C. Walking Ability

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

D. Normal Work (includes both work outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

E. Relations with other people

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

F. Sleep

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

G. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

reproduced for inclusion in the patient's chart, records the location of each pain (on a diagram); the worst, least, and average pain intensity, as well as the level "right now"; the degree of relief that pain treatments have provided; and the functional consequences of the pain.

The functional consequences, such as disturbances in physical activity, mood, walking ability, relationships with others, sleep, and enjoyment of life, can be sensitive indicators that a patient's pain is unrelieved. Even patients who cannot tell you whether their pain number has changed, or cannot give you a word to describe it, report changes in their functional levels that indicate the efficacy of the treatment. Patients' families can help as well, completing the assessments at home after changes in the patient's pain-relief regimen and reporting the results to you by phone or e-mail.

The functional changes noted in Mr. Cirelli's behavior, for example, heralded the relief of his pain. From a bedridden, depressed, withdrawn person with a short temper and attention span, he became voluble, helpful, interactive, and cooperative. When his pain was relieved, the disturbances disappeared.

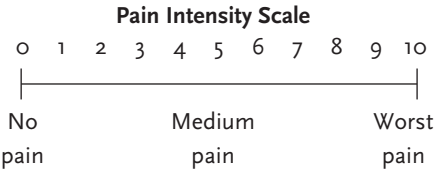
Pain Diaries

The VAS, word scales, MPAC, and Wisconsin Brief Pain Inventory provide sufficient information for designing pain-relief regimens for most patients. But there can be cases in which the regimen seems to be working only part of the time. Pain diaries, which can be as high tech as a smartphone app (Rosser and Eccleston 2011; Jacob et al. 2013) or as simple as pen and paper, are useful here. In the diary, patients record the time of day they took their pain medicine, the pain intensity rating before and after they took it, the type of pain medicine, and any other comments they feel are relevant (e.g., what they were doing when the pain occurred). A sample diary page is shown in Figure 5.6.

For patients who complain of being too sedated, diaries can help determine whether they're taking too much medicine, or taking the correct dose but too often. And diaries are useful for patients who have *breakthrough pains,* moderate to excruciating acute pains that occur intermittently, often on a background of well-controlled chronic pain. There are three types of breakthrough pain: *end-of-dose pain,* which is pain that recurs before the next regularly scheduled dose of medication is due; *incident pain,* which is directly related to an activity (such as turning over in bed); and *spontaneous pain,* which occurs unpredictably.

Diaries are helpful in determining which kinds of breakthrough pains patients are experiencing. For many, the pattern that emerges will reveal end-of-

You can use a chart like this to rate your pain and to keep a record of how well the medicine is working. Write the information in the chart. Use the pain intensity scale to rate your pain before and after you take the medicine.



Date	Time	Pain intensity scale rating	Medicine I took	Pain intensity scale rating 1 hour after taking the medicine	What I was doing when I felt the pain
9/1/14	*2:35*	*6*	*2 ibuprofen tablets*	*3*	*Sitting at my desk and reading.*

Figure 5.6. Pain diary. From the Agency for Health Care Policy and Research, Rockville, Md.

dose pain or incident pain. You can then devise a plan to prevent the anticipated pains. For example, if the pain recurs four hours before the next sustained-release morphine pill is due (i.e., end-of-dose pain), you can decrease the dosing interval to eight hours. Or if a patient's pain reliably exacerbates with movement (i.e., incident pain), a short-acting medication can be given thirty minutes to an hour before the patient gets out of bed, or an immediate-acting agent can be given five or ten minutes before.

Finally, diaries are essential to solving the mysteries of those few patients who have a pain recurrence pattern that seems to make no pharmacologic sense. Miss Alexander was such a patient.

The Pain Pattern That Makes No Sense

Miss Alexander was a 32-year-old woman receiving chemotherapy for metastatic ovarian cancer. She had worked in her father's business since her high school graduation and had lived in her own apartment until the side effects of the chemotherapy and increasing disability from her cancer forced her to move back to her parents' home.

Miss Alexander had abdominal pain that, despite my efforts at changing her medication dose and schedule, seemed never to come under satisfactory control. I asked her to keep a pain diary. In the diary she recorded that she took sustained-release morphine at 6 a.m., 2 p.m., and 10 p.m. At 7 a.m., before setting out for work, she usually took a dose of immediate-acting morphine. Using a scale of 0 to 10, she recorded her pain intensity before each dose of morphine and its intensity an hour or so later.

She had been taking the same morphine doses for about a week when she came to the office. I reviewed the diary and graphed the pain intensity (0 to 10) on the *y* axis and the time of day on the *x* axis (Figure 5.7). I noted that her pain intensity was highest on weekends and between 7 p.m. and 10 p.m. on weekdays. Her pain relief was satisfactory at all other times.

There is nothing I know about morphine's pharmacology that could explain why sustained-release morphine would be effective for eight hours in the daytime on weekdays and overnight, but not on weekends or weekday evenings. As I wondered what other factors might be involved, I considered that it might be difficult for Miss Alexander, a formerly independent, lively young woman, to have to return from work to her conservative family home every night and weekend. So I questioned her about this. She replied,

When I'm at Dad's office, there's plenty to keep me occupied. I do some work, though not as much as before, and I can visit with my friends. But there's not much to do at

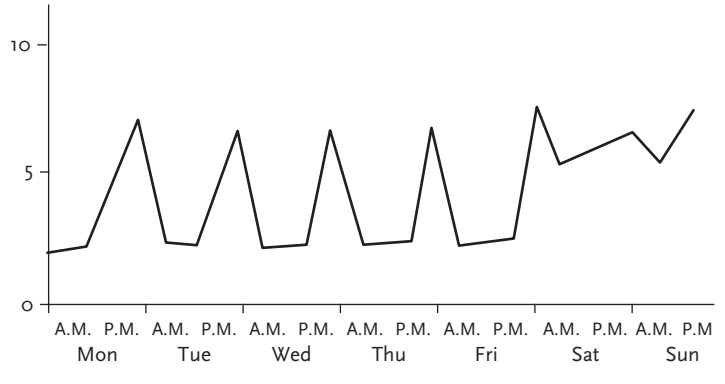


Figure 5.7. Miss Alexander's pain pattern.

home. And Mom keeps asking me all the time, "How are you doing? Are you having any pain? Is there anything I can get you?" or "What did the doctor say today, honey?" Oh, sometimes there's a TV program I like, or I can get caught up in a book I'm reading. The pain's not so bad, then—kind of like it is at the office. But most of the time, it's much worse.

At home, it seemed, there wasn't much to take her mind off her cancer or her loss of independence, and her pain was more intense and caused her more distress. Since she had found a few things that helped, I suggested she try to continue to fill her evenings and weekends watching movies or videos, listening to music, or reading books on her iPad, and to ask her friends from the office to visit or take her with them on weekend outings. Happily, this strategy was effective, and her pain came under satisfactory control without any further changes in dose or timing of medication. The diary was the key—once I knew *when* it hurt, I could figure out *why*.

Comprehensively Evaluate the Patient

Further questioning includes exploring (1) the temporal aspects of the pain (is it acute, chronic, or breakthrough pain?), (2) its quality (is it somatic, visceral, or neuropathic?), and (3) its similarity to pain syndromes typically seen in cancer patients. Depending on the causes you think likely, other diagnostic tests should follow. Finally, to uncover sources of anxiety and distress not caused by pain (but potentially making the pain worse), patients are evaluated for psychological, social, financial, and spiritual problems.

Temporal Aspects of Pain: Acute, Chronic, or Breakthrough

Cancer patients usually have a mixture of chronic and breakthrough pains. To maximize pain relief while minimizing side effects, it is useful to determine both the intensity of the chronic pain and the characteristics of the breakthrough pains and to treat each with agents appropriate for them.

Long-acting agents (e.g., methadone) or sustained-release formulations of short-acting agents (e.g., transdermal fentanyl or buprenorphine, sustained-release oxycodone, morphine, oxymorphone, or hydromorphone) are used to keep the chronic pain at an acceptably low level (e.g., level 2 or 3). The peak blood level of opioids delivered in these preparations is lower than with the other formulations and they are therefore less sedating.

End-of-dose breakthrough pains, once recognized, are easy to prevent by increasing the frequency of dosing of sustained-release agents. Spontaneous pains and incident pains, which can be precipitated by movement, the Valsalva

maneuver, or even flatulence, are more difficult to manage. A patient with bony metastases, for example, may have reasonable control of chronic pain without excessive sedation but develop severe pain when rising from a bed or chair. Agents with a quick onset of action (hydromorphone, morphine, oxycodone, and oxymorphone) and immediate-acting agents (the transmucosal formulations of fentanyl citrate) can be added either prophylactically for activities expected to cause incident pain or episodically when spontaneous pains occur. But the higher peak opioid levels associated with these agents can cause sedation. Patients often must endure this increased sedation to achieve acceptable pain relief.

Pain Quality: Somatic, Visceral, or Neuropathic

Determining the quality of cancer pain is often helpful in identifying the site of tissue injury, because somatic, visceral, and neuropathic pains each have a characteristic presentation. Somatic and visceral pains are common in people who do not have cancer. Other than in patients with disk disease, diabetic or alcoholic neuropathy, or herpes zoster, however, lesions that cause neuropathic pain rarely occur in people who do not have cancer or AIDS.

Somatic pain. Somatic pain arises from skin and subcutaneous tissues, bone, muscle, blood vessels, and connective tissues. It is usually described as *constant, dull,* and *aching, increased by movement,* and *localized to the area of the lesion.* Patients with arthritis or bony metastases will describe their chronic pain in words similar to these. Incident pain, however, is not dull but rather a sharp, intense somatic pain caused by movement of a bone containing a metastasis.

Visceral pain. Visceral pain arises from organs and the lining of body cavities. The pain caused by a myocardial infarction is a typical example of visceral pain. It is often a *poorly localized, deep, aching* discomfort, but it can feel like *cramping, squeezing, twisting,* or *tearing.* Patients with hydronephrosis caused

PRACTICE POINTS: DISTINGUISHING AMONG SOMATIC, VISCERAL, AND NEUROPATHIC PAIN

- Somatic pain (e.g., arthritis, bone metastases) is constant, dull, and aching, increased by movement, and localized to the area of the lesion.
- Visceral pain (e.g., myocardial ischemia, liver metastases) is poorly localized, deep, aching, cramping, twisting, or tearing.
- Neuropathic pain (e.g., sciatica, brachial plexus metastases) is burning, sharp, shooting, tingling, electrical, or shocklike.

by tumor or a distended liver filled with metastases will have this type of pain. Visceral pain can localize to more superficial structures and, if it is intense, often radiates to larger areas, usually the muscle or skin innervated by the same spinal nerves that innervate the viscus. Pain in the left shoulder and arm of a patient with myocardial ischemia is an example of this phenomenon. Abdominal pains due to bowel obstruction by tumor also are visceral, but they have the intermittent, cycling quality that characterizes an obstruction from any cause.

Neuropathic pain. Neuropathic pain, the kind from which Mr. Cirelli was suffering, arises from peripheral nerves, the spinal cord, and the central nervous system. It is the most distressing type of pain. Neuropathic pain is usually poorly localized; it is often *burning* (as typically seen in diabetic neuropathy or herpes zoster) but can be described as *sharp, shooting, tingling, electrical,* or *shock-like.* With sufficient nerve damage, there may be associated *paresthesias, painful numbness, hyperesthesia,* or *sensory loss,* and, as in Mr. Cirelli, *weakness* and *muscle wasting. Allodynia,* pain caused by normal touch or by clothing, or *hyperalgesia,* a mildly painful stimulus causing severe pain, can also occur. Neuropathic pain can be limited to the site of the lesion, but it often radiates or is completely referred to distant sites.

Recognizing Cancer-Related Pain Syndromes

Cancer-related pain syndromes are most often caused by nerve damage. The cancer usually has spread to the bone or tissue adjacent to the nerve, and as it grows, it compresses the nerve or its blood supply, causing neuropathic pain and eventual nerve death. Recognizing neuropathic pain, therefore, is crucial to identifying patients with lesions of (1) cranial nerves as they exit the skull, (2) nerve plexi (cervical, brachial, and lumbosacral), (3) peripheral nerves, and most dangerously, (4) the spinal cord (from tumors in vertebral bodies and the epidural space) (Foley 1987).

Cranial nerves. Metastases to the *jugular foramen* cause occipital and ipsilateral shoulder pain along with dysfunction of cranial nerves 9 to 12, which exit through the foramen. Disease of the *sphenoid sinus* mimics sinusitis, but patients with tumor infiltration usually have a more severe headache, and they may have diplopia due to infiltration or edema of the sixth cranial nerve. Patients with tumor infiltration of the cranial nerves have pain in the head and face in the distribution of the nerve involved, often the ninth or the trigeminal.

Nerve plexi. Brachial or lumbosacral plexus infiltration can be particularly difficult to diagnose, but it can herald primary or recurrent tumors. In the brachial plexus, the nerves lower in the plexus (C7 to T1) are most likely to be directly invaded by tumor, as were Mr. Cirelli's. Patients with either brachial or lumbosacral plexus infiltrations present, as did Mr. Cirelli, with deep, aching, often shooting

pains and, later, muscle atrophy in the groups innervated. MRI (magnetic resonance imaging) may reveal tumor infiltration, and treatment can be planned.

The pain of radiation fibrosis may mimic that of recurrent cancer in the brachial plexus, but it has a different distribution. Because the clavicle protects the nerves lower in the plexus, nerves located in the upper part of the plexus (C5 and C6) are most commonly affected by radiation damage. The pain and weakness will be in the C5,6 distribution; an EMG (electromyogram) will document the abnormality.

Peripheral nerves. The *post-mastectomy* and *post-thoracotomy* pain syndromes are caused by diseases of peripheral nerves. Prompt recognition of these syndromes is particularly important because treatment within six months of their onset is usually very effective.

The term *post-mastectomy* syndrome is something of a misnomer because it can occur in women who undergo any type of breast surgery, from lumpectomy to radical mastectomy. It is a common problem: 4 to 10 percent of women who undergo breast surgery develop this syndrome. The pain can appear immediately or as late as six months after the surgery. A patient with post-mastectomy syndrome feels a burning, constricting sensation in her posterior arm, axilla, and anterior chest wall in the area where she has lost sensation due to the surgery. Her chest wall may be hyperesthetic or dysesthetic. The patient finds it most comfortable to keep her arm flexed, and she may therefore develop a frozen shoulder. Post-mastectomy pain is caused by a neuroma of the intercostobrachial nerve (a branch of T1,2), which was cut during surgery. There is often an associated trigger point (a place where the pain can be reproduced by touching that part of the skin) in the axilla or anterior chest wall.

Similarly, patients who have had thoracotomies or who have ports inserted for intravenous access can develop post-thoracotomy syndrome. These patients describe an aching and burning sensation in the distribution of the incision and numbness of the skin in that area. There is exquisite point tenderness at both ends of the scar. The post-thoracotomy syndrome is caused by pulling or cutting of the intercostal nerves.

As you can imagine, suffering caused by either of these syndromes can be significant, especially for those whose cancer has been cured. For these patients, the pain is a reminder both of the experience and of the potential for cancer recurrence. Early diagnosis and prompt treatment can eliminate this pain.

Vertebral lesions. Patients with *odontoid* and *atlas* fractures present with severe neck pain radiating over the posterior part of the skull to the vertex as well as neck stiffness. The symptoms may mimic meningitis and are particularly dangerous because the patient is at risk for developing paraplegia or quadriplegia from the subluxation and spinal cord or brainstem compression.

Metastases to C7 often do not cause neck pain, but patients experience pain between the scapulae. Early detection will prevent cervical cord compression, but these lesions are often missed because films are taken only of the thoracic spine, and if the findings are normal, no bone scan is done. Similarly, *lesions of T12* can present as isolated hip pain, as occurred in Mr. Young. Here also, if hip, pelvis, and thoracic spine films reveal no abnormalities, a bone scan is indicated. For either lesion, CT (for surgical therapy) or full spinal MRI (for radiation therapy) will be required to plan therapy. The C7 and T12 referred pain syndromes are important to recognize but are rare.

Epidural disease in cancer patients usually does not cause a unique pain syndrome. It presents most commonly as back pain in the area of the vertebral metastasis, with or without radiation in the distribution of the spinal nerves exiting the spinal cord at that level. Its similarity to the pain of benign disk disease is a source of dangerous diagnostic confusion.

PRACTICE POINTS: RECOGNIZING SPINAL CORD COMPRESSION

- Back pain may be the only finding.
- In a patient with back pain and findings consistent with metastases on a plain film of the spine in the area of the pain, the probability of invasion of the epidural space is approximately 70 percent. A radiculopathy raises this probability to 90 percent.
- Emergency MRI is indicated in any cancer patient with back pain, even when the neurologic exam is completely normal.
- Prompt recognition and therapy is the key to preserving ambulation; only 10 percent of patients with spinal cord compression who lose their ability to ambulate will ever regain it.

If a patient without cancer complains of back pain and there are no abnormal neurologic findings, most physicians would not order a plain film of the spine, let alone an MRI. They would treat him symptomatically. But in a cancer patient, back pain may be the only clue that he has a malignant epidural process and an impending cord compression. Thus evaluation of the back pain of a cancer patient must be much more aggressive than that of the patient without cancer.

Even with completely normal neurologic findings, an MRI must be done to exclude epidural disease in a patient with back pain and cancer, whether active or dormant. In fact, there is about a 70 percent chance that a cancer patient with back pain and abnormal plain films of the spine has epidural metastases. This very important

fact is not widely known, and many physicians wait for abnormal physical findings before pursuing further diagnostic tests. Some let the decision rest on the results of the bone scan, but as many as 5 percent of cancer patients with normal bone scans will have metastatic bony disease demonstrated on MRI. Bone scans are of little value as a screening test for patients with multiple myeloma, because the results are usually normal even in the presence of extensive bony disease.

MRI of the entire spine should be obtained immediately (Janjan 1997, Abrahm et al. 2008, Mehta and Arnold 2011). MRI is as sensitive and specific as CT myelography, which is a more uncomfortable procedure and potentially associated with more complications. Further, in 40 percent of patients whose cancer involves more than one epidural site, an MRI will reveal additional lesions above and below the area of pain, which may make the patient ineligible for surgery and will need to be included in the radiation field (Abrahm et al. 2008).

Epidural metastatic disease must be diagnosed and treated before any neurologic abnormalities develop, because once they appear, they are often irreversible. If patients are treated while they are still ambulatory, they have about a 90 percent chance of remaining so. If they become paraparetic, the odds drop to 40 to 50 percent, and only 10 percent of patients who lose their ability to walk because cancer is compressing their spinal cord will ever walk again.

Psychological, Social, Financial, and Spiritual Sources of Anxiety or Distress

Asking *"How are you within yourself?"* (Byock 1997) is a wonderful way to start a conversation designed to detect the psychological, social, financial, or spiritual problems that often occur in cancer patients with pain and that by themselves can cause distress even in those without pain. An evaluation in each of these areas completes the initial pain assessment. And, because patients' reactions to pain are modified by their families' reactions and abilities to cope with someone in pain, a determination must be made of how the family is functioning. For patients cared for by hospice teams, the nurse, social worker, and chaplain will routinely do these assessments and communicate the results to you.

The model developed by Betty Rolling Ferrell, PhD, RN, FAAN, associate research scientist at City of Hope National Medical Center, provides a framework for the assessment (Figure 5.8). This model explores the extensive effects of pain on all dimensions of the quality of a patient's life: physical, psychological, social, and spiritual (Ferrell and Rhiner 1991). We have already reviewed how to assess the physical impairments induced by pain; I discuss here how to assess the psychological, social, and spiritual causes.

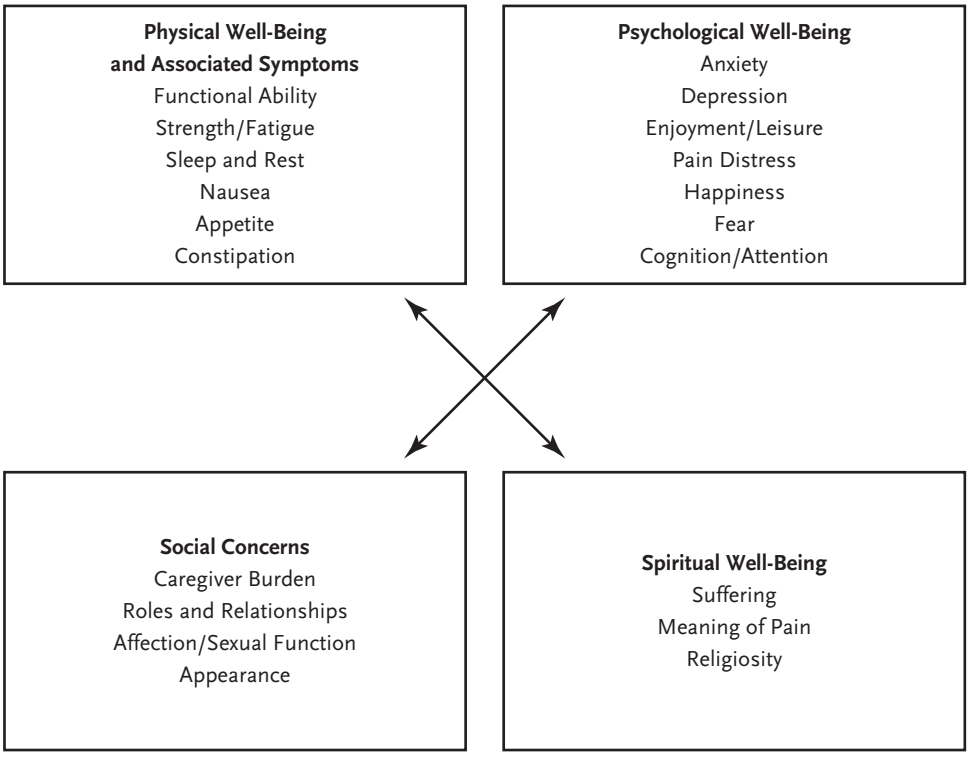


Figure 5.8. Effects of pain on dimensions of the quality of life. From B. R. Ferrell and M. Rhiner, High-tech comfort: ethical issues in cancer pain management for the 1990s, *Journal of Clinical Ethics*, 2:108–112, 1991; copyright 1991 by *The Journal of Clinical Ethics*; all rights reserved.

Psychological causes. Psychological effects of cancer pain include both the emotional response to the pain (the affective dimension) and how the patient thinks about the pain (the cognitive dimension). Delirium, an organic mental disorder that particularly affects cancer patients, is rarely caused by the pain itself but is a source of great distress.

Affective Dimension. People who have uncontrolled pain are usually unable to feel much pleasure. Happiness, even of a momentary kind, is very hard for them to imagine. In addition, patients in pain are often anxious or depressed and are unable to focus their attention on anything other than the pain. Pain also exacerbates depression, which is the strongest contributing factor to suicidal ideation in cancer patients.

Anxiety and depression are, of course, not limited to cancer patients with pain—they are the most common psychological problems of all patients with

cancer. Assessment and management of patients with depression and anxiety are discussed in Chapter 9.

Cognitive Dimension. The cognitive dimension, which includes families' and patients' attitudes, beliefs, and knowledge about pain and its treatment, affects their interpretation of new pains and their acceptance of proposed changes in treatment regimens. For example, it may be psychologically easier for the family to ignore worsening pain than to face the implications of the patient's worsening condition. In their denial of the patient's impending death, they may not adequately treat his escalating pain. Families are no better than physicians at guessing the intensity of the patient's pain, and the more different their perception is from what the patient is actually feeling, the more stress they experience (Miaskowski et al. 1997).

PRACTICE POINTS: ASSESSING OTHER DIMENSIONS OF THE PAIN EXPERIENCE

- Discover what the pain means to the patient; it will affect both emotional response to pain and ability to cope with it.
- Determine the patient's expectations about the extent of pain relief and work to align these expectations with what you know to be clinical reality.
- Assess the family caregiver's personal characteristics (e.g., age, sex) and how those characteristics affect caregiving efforts, especially as they relate to giving pain medications.
- Assess the family's willingness to acquire new skills, desire for information, and psychological needs.
- Take the opportunity to reassure the patient and family that the patient's pain will be controlled and that the family will be supported in its caregiving efforts.

Gaining a family's cooperation begins with assessing its desire for information, willingness to acquire new skills, and psychological needs. Physicians can begin this process by addressing unasked family questions, such as:

How bad is his pain likely to get in the future?
Will we have help managing Mom's pain at home?
Who will answer our questions as they arise?

Family members can be reassured that you will be able to relieve the pain, no matter how intense it becomes, and that you will not abandon them. They will

know that you'll work with them and help them cope with the stresses they are likely to experience as they care for the patient at home.

A number of personal characteristics can help you anticipate how caregivers are likely to help manage the patient's pain. Younger couples, for example, are more likely to be frustrated and angry, but they are less likely than older couples to be overwhelmed and feel depressed. Women tend to experience and express more distress and depression but are more understanding of the patient's physical and emotional needs, while men focus on financial matters and household chores.

In addition to the family assessment, you also need to know what patients are thinking and feeling. You have to determine what the pain means to them, because this will affect their emotional response to and ability to cope with the pain. Does the patient, for example, believe his pain to be a manifestation of progressive disease? People who have this belief are more likely to be depressed or anxious or to report more pain than those who do not. Alternatively, the patient may regard his pain as a challenge. If so, he will probably cope better and be less depressed than someone who views pain as a punishment.

You must also ascertain patients' therapeutic expectations. A patient with extensive bony metastases is unlikely to achieve complete pain relief without side effects if the only medication she takes is a sustained-release morphine preparation. She may have such an expectation, however, and question the polypharmacy that is prescribed. Once the source of confusion is elicited, the patient's expectations can be better aligned with yours.

Presentations of Delirium. Delirium is the most common organic mental disorder affecting cancer patients. While rarely caused by pain, delirium can be caused by the medicines used to treat it, and it can present as uncontrolled pain. Metabolic disruptions and the dying process itself also cause delirium. Miss Monroe was a patient of mine when I was practicing hematology and oncology; she experienced delirium from a number of causes.

The Problem of Delirium

Miss Monroe was a 62-year-old elementary school teacher who developed multiple myeloma. She was sent to me from her general internist, who had made the diagnosis during his evaluation of her complaints of back pain and anemia. MRI revealed that her pain was due to an epidural spinal cord compression, and she was just finishing radiation therapy for this when she had her first episode of delirium.

Miss Monroe was accompanied on her visit by her niece, Samantha, who lived with her while going to college. Samantha had noted that her aunt was not always herself these days. Miss Monroe had previously been a very steady, matter-of-fact

kind of person, friendly, generous, and caring. Her students loved her, and her colleagues respected her. Lately, however, her behavior had become erratic. Although much of the time she seemed her old self, at other times she appeared euphoric, at others depressed and tearful, and at still others angry for no apparent reason. She forgot things she never would have forgotten before and seemed increasingly distant. Samantha missed the nightly talks they used to have about school and the strategy sessions for getting through the next day or week.

What Samantha had noticed were the early signs of delirium. Miss Monroe's memory was impaired; she wasn't thinking clearly; she had poor judgment; and her mental status varied from normal to abnormal throughout the course of the day. Because her calcium, sodium, and blood glucose levels were normal, we believed her delirium was caused by the high-dose corticosteroids she had begun taking when her spinal cord compression was diagnosed. Steroid-induced delirium is by no means rare: in one study, as many as one-quarter of the cancer patients treated with high-dose prednisone or dexamethasone developed delirium.

Because her radiation therapy treatments were completed, her corticosteroids were tapered rapidly—and her mental status quickly returned to normal. But later in the course of her illness, she had progressive bony disease that was refractory to therapy and began taking sustained-release morphine preparations for the pain. When the dose was escalated to improve pain control, Miss Monroe herself noticed a problem.

"I think I must be going crazy," she told me at one clinic visit. *"A few months ago I was having nightmares, but that sort of made sense to me. After all, I'm under a lot of strain here; my cancer seems to be getting worse and not better, and a few bad dreams were not something I even considered mentioning to you. But lately, I'm seeing things that Samantha doesn't see and talking with people I know can't be real because they died years ago! What is happening to me?"*

Once again, Miss Monroe was suffering from delirium, manifested this time by hallucinations. The morphine was responsible. Her earlier nightmares had been caused by the morphine, and raising her dose had made the problem even worse. Her symptoms disappeared when she was switched to a different opioid.

Her final bout with delirium occurred as she was dying at home. She had declined hospice services, and Samantha was doing the bulk of the caregiving. Samantha called me in tears one night at 3 a.m. to report a sudden major change in her aunt. Earlier that day Miss Monroe had been resting comfortably. Now, when Samantha had tried to give her some pain medication, she had refused and accused Samantha of trying to poison her. Samantha wasn't even sure that her aunt recognized her. Miss Monroe was restless, throwing off the bedcovers or "picking" at them, and was shouting at her, swearing, and refusing to be touched.

Samantha said that she was about to call the police but thought maybe I had some idea of what was going on.

I told her that the symptoms and signs indicated that her aunt had another, more severe form of delirium: Miss Monroe was confused and disoriented; her speech was not always coherent; she got worse at night; and she had no insight into her problem. I reassured Samantha that none of this was her fault, that over three-quarters of dying patients experience delirium. I advised her on which medication to administer. Luckily, Miss Monroe responded promptly. Three days later, she died peacefully at home.

During her illness, Miss Monroe displayed many of the symptoms of a hyperactive delirium, which occurs in about a third of delirious patients: agitation, hallucinations, disordered thinking and perception, delusions, labile mood, and what is termed "psychomotor behavior"—picking at bedcovers, for example. Another third of delirious patients, however, experience a quiet delirium that can go undetected unless sought. Such patients are not agitated—they may be resting quietly in bed, but when asked, they may have paranoid ideation, or may confirm that they do not feel safe. The final third show evidence of both hyper- and hypoactive delirium. Delirium in any of its presentations is distressing and requires therapy. Almost three-quarters of delirious cancer patients who recovered remembered their experience and found it profoundly distressing (Hui et al. 2010).

The causes of Miss Monroe's delirium included corticosteroids, opioids, and the terminal illness itself. She did not receive lorazepam (Ativan), which, paradoxically, can cause an agitated delirium. She was also not receiving anticholinergic agents, which, when combined with drugs with anticholinergic side effects, can cause a "cholinergic crisis," a life-threatening syndrome that includes high fevers and delirium. H_2 blockers (e.g., cimetidine), tricyclic antidepressants, and anticholinergic agents (e.g., diphenhydramine [Benadryl] or hydroxyzine [Atarax, Vistaril]) all have significant anticholinergic side effects and can contribute to a cholinergic crisis.

Other causes of delirium include structural brain lesions, encephalitis, hypoxia, hypercalcemia, renal or hepatic failure, electrolyte imbalance, nutritional deficiency (especially of B vitamins), and infection. As I discuss in Chapters 6 and 9 delirium from a number of these causes can often be treated effectively, even when the underlying problem cannot be reversed.

Role of the Mental Health Professional. Immediate referral is needed to assess and treat the patient who is suicidal or who is delirious but not actively dying. For the more routine patient with anxiety or depression, however, a formal psychological evaluation is not always needed. If pain is controlled but the patient

is still anxious or depressed, a trial of one of the psychoactive medications discussed in Chapter 6 is often successful. If this is ineffective, patients often benefit from seeing a psychologist or psychiatrist. As is reviewed in Chapter 9 their anxiety and depression often respond to the therapy and ongoing support these professionals provide.

PRACTICE POINTS: ASSESSING DELIRIUM

- Delirium is characterized by:
  - —a change in cognition that cannot be explained by dementia.
  - —a disturbance of consciousness with reduced ability to focus, sustain, or shift attention.
  - —a disturbance that develops within a short time and fluctuates throughout the day.
- Symptoms include insomnia and daytime somnolence, nightmares, irritability, distractibility, hypersensitivity to light and sound, anxiety, difficulty in concentrating or marshaling thoughts, hallucinations, delusions, emotional lability, attention deficits, and memory disturbances.
- Patients may appear hypoactive, depressed, or extremely agitated.
- Precipitating factors include metabolic derangements (hypercalcemia, hypo- or hyperglycemia, hypo- or hypernatremia, hypoxia, renal or hepatic failure), drugs (especially opioids, corticosteroids, and anticholinergic agents), nutritional deficiency (especially of B vitamins), infection, structural brain lesions, and encephalitis.

Social and financial causes. Some patients are suffering from what Cassell, in *The Nature of Suffering and the Goals of Medicine*, describes as a loss of "personhood." Cassell has developed a "topology of person" that explores the many dimensions of how illness can affect an individual's personhood and cause suffering. Personality and character will affect the response to illness, as will "the lived past . . . a story that has taken place over time, in many places, and involving countless others" (2004, p. 43) as well as the family's lived past. The patient's cultural background, the many roles he has played (son, father, Little League coach, board chairman), and his associations and relationships are also determinants of suffering in response to illness. Grief over having to relinquish these activities and the accompanying loss of social standing can be a source of significant pain. Other sources include injuries to the body or unconscious mind, diminished possibilities of the self as a political being, loss of a secret life, dashed hopes for the perceived

future, or loss of the transcendent dimension—the spirit. When disease progresses, these aspects of personhood may become damaged or lost. Knowledge that these roles may never be regained becomes an ongoing source of suffering.

Patients and their families also need an evaluation of the social and financial barriers to optimal pain relief. A basic assessment should include the family's living conditions and financial and insurance status. This information helps to determine, for example, whether financial help will be required for patients who need the more expensive pain medicines or a high-tech pain therapy, such as intravenous or epidural opioid infusions. It will also reveal whether financial worries are causing insomnia, which exacerbates pain. Determining whether the pharmacies where the patients live will order the opioids the patients need is also important. Studies have shown that pharmacies in neighborhoods housing mainly nonwhite patients are much more likely not to stock or agree to order opioids (Morrison et al. 2000). A 2000 survey of 347 New York City pharmacies showed that the higher the proportion of nonwhites in the population, the lower the availability of opioid analgesics.

Cultural Context. Physicians will benefit from understanding cultural and religious aspects that affect patients' and families' attitudes toward cancer and pain and their ability to communicate their distress. Japanese and Italians, for example, have been found to associate cancer with death. If an Italian patient has pain caused by the cancer, it might serve as a trigger for thoughts of impending death, which would in turn exacerbate the pain experience. In other cultures, the social expectation is that pain should be tolerated; patients in such environments face disapproval from their families if they complain of pain. If you were unaware of the social pressures that led a patient to minimize his pain, you might easily underestimate his true pain intensity.

Similarly, religious teachings may affect a patient's preferences for pain therapy—a Buddhist, for example, may resist strong pain medication because she thinks it will weaken her spirit or cloud her consciousness sufficiently to impair her preparations for dying. An Orthodox Jew may refuse opioids fearing they will hasten his death, and he does not wish to do anything to shorten the life that God has given him.

Several questions can help us assess the cultural and religious attitudes, beliefs, and coping styles of patients and their families (Fong 1985). Answers to these questions should give us a better idea of how the patient and family communicate about pain and how they wish us to treat it.

Family Disruption. Other social sources of distress arise from disruptions in a person's normal family structure and her place in the community when she becomes a cancer patient. The entire family organization may be turned

topsy-turvy when the person who was the breadwinner (or the homemaker) can no longer serve in that capacity. Others must take over her tasks, which puts both social and financial stress on everyone in the family, including the person who has had to relinquish her accustomed role.

Role of the Social Worker. Hospital social workers, the social workers employed by home health agencies or hospice agencies, or those in oncology practices effectively perform comprehensive assessments of patients' cultural and psychosocial needs and obtain help for families dealing with these issues. Even if families do not directly express these types of concerns, encourage them to have at least one consultation with the social worker. This consultation often allows the social worker and the patient's family to develop a relationship that can be renewed as needed throughout the course of the patient's illness.

At the time of diagnosis and during the early phases of treatment, in addition to performing the psychological and social assessment, social workers may

PRACTICE POINTS: QUESTIONS FOR ASSESSING CULTURAL ATTITUDES OF PATIENTS AND THEIR FAMILIES

- Is touching acceptable to you?
- What word do you use for pain?
- How will we know you are in pain?
- How does your family usually react to pain?
- How do you normally treat or cope with pain?
- Which foods are comforting or healing to you?
- Do you want your family near you when you are hurting?
- How does your family react to your pain?
- Do you see a folk healer when you are sick?
- How do you explain your illness or pain?
- What does the pain mean to you?
- Does the pain mean you are getting better or worse?
- Is it OK to take medication to relieve pain? If not, why?
- Do you want immediate pain relief or do you believe that you must wait until the pain is severe?
- What type of treatment do you want to control your pain?
- Do you read? Which languages?
- How best do you learn (reading, videos, etc.)?

(From Fink and Gates 1995, 34)

assist in treatment planning, solve insurance and other financial problems, and connect the patient and family with community social service agencies. Social workers can also advise you as to which families or patients need more intensive psychological support. They may themselves be able to provide the needed counseling and education in coping skills. If the disease later progresses, the social worker can continue to provide the patient and family members with psychological and social assessments and, for those who need it, intensive counseling or assistance in coping with impending death. I discuss these therapeutic roles of the social worker in more detail in Chapter 9.

Spiritual causes. Spiritual well-being can modify the experience of pain. Studies have shown that although religious patients reported pain as often as those who were not religious, their pain levels were lower. Moreover, their anxiety, pain frequency, and pain intensity declined as their level of spiritual well-being increased. Studies indicate that more generally, religion and spirituality are important sources of hope and coping for patients at the end of life, and that spirituality "preserves patients' quality of life despite severe physical symptoms, supports prognostic acceptance, and protects against hopelessness and despair near death" (Phelps et al. 2012, p. 2538). The Religion and Spirituality in Cancer Care Study, a multi-institution, quantitative and qualitative study of 75 patients with advanced cancer and 339 cancer physicians and nurses, found that patients reported being provided with spiritual care only 25 percent of the time, although 77 percent of patients, 72 percent of physicians, and 85 percent of nurses thought it would be beneficial. In the setting of terminal illness, 41 to 94 percent of patients want their physicians to include attention to patients' religious and spiritual needs, and such attention is included in national palliative care guidelines (Phelps et al. 2012).

Suffering and the Meaning of Pain. *Suffering* and the *meaning of the pain* are two areas that are of particular importance to patients who have been referred to me with uncontrolled pain. They seek meaning for their suffering in the context of their religious teachings, and they need to understand the meaning of their pain. Religious beliefs can have a profound effect on a patient's interpretation of his pain and suffering. Physical pain can exacerbate spiritual concerns, increasing the need for comfort and forgiveness or creating anger at what is perceived as abandonment in a time of need.

Spiritual assessment is not the sole province of the hospital chaplain. Nurses, social workers, and physicians can all assess patients and their families using one of several assessment tools, including many designed specifically to determine the interaction of pain and spiritual suffering (Taylor and Ersek 1995) or to identify the presence of spiritual suffering even in the absence of

pain (Fitchett and Handzo 1998). The FICA scale, also easy to use, has been extensively validated in research studies (Pulchalski and Romer 2000). As Dr. George Fitchett states, "The aim of spiritual assessment is not to exhaust the complexity or mystery of the spiritual dimension of life. The aim is to organize observations about people's spiritual beliefs, behaviors, and relationships in ways that enhance caregiving" (p. 791). His "7 × 7 model" incorporates spiritual assessment as part of a "holistic" patient assessment, which includes the biological (medical); psychological; family system; psychosocial; ethnic, racial, and cultural; social; and spiritual dimensions. His spiritual assessment tool includes a variety of components that taken together describe the spiritual life of the patient. These include:

- *Belief and Meaning,* and affiliation with a formal religion.
- *Vocation and Obligation,* as these relate to beliefs and sense of meaning.
- *Experience and Emotions,* which identify reactions to direct contact with the sacred, divine, or demonic.
- *Courage and Growth,* which determine the rigidity of the current belief system and willingness to adapt it to new challenges.
- *Ritual and Practice,* which the patient feels should be performed.
- *Community,* including the patient's affiliations and the nature of his participation.
- *Authority and Guidance,* which identify the source of authority for the patient's beliefs and his resources (including himself) in times of stress.

I have heard various answers to the questions developed by Fink and Gates (1995) to determine the interaction of pain and spiritual suffering. Many

PRACTICE POINTS: QUESTIONS FOR REVEALING INTERACTIONS OF PAIN AND SPIRITUAL SUFFERING

- What do your religious teachings say about pain?
- Have your beliefs or values changed since you began having pain?
- Where do you get the strength to live with your pain?
- Do you find any value to living with suffering—has it ennobled you in any way?
- Does the pain affect your ability to practice your religion—does it, for example, interfere with prayer or attending church?
- Does the pain affect your relationship with God?

(From Fink and Gates 1995, 52)

patients have told me that they had searched their consciences for reasons that God was allowing them to suffer. They felt they were being punished, as they had been as children when they had done something wrong, but they could not think what they had done to deserve such punishment. Some veterans have concluded that it was something they did in the war, saying that they wanted to "burn here" so they wouldn't have to "burn there" (see Chapter 2). They supposed the pain had to be a "just punishment" for their sins. Others have found deficiencies in their former relationships with other people or with God. In many who could find no cause for their suffering, a previously deep faith was profoundly shaken and its comforts were suddenly gone. They told me they felt alone and abandoned.

Role of the Spiritual Counselor. These people need spiritual counseling and forgiveness if their suffering is to be ameliorated. Chaplains are key members of the hospice team, and our hospital, like many others, has on its staff specially trained non-denominational pastoral counselors who can discuss with patients their feelings of abandonment by God and of punishment for unknown offenses, their fears of death or the afterlife, or their need for prayer or sacraments. Many patients want to know what they need to do to resolve outstanding spiritual issues before they die; for some this includes a confession or the resolution of outstanding arguments with friends or family members; for others, a marriage in the hospital room. For some, Dr. Ira Byock's "Five things of relationship completion: 'I forgive you'; 'Forgive me'; 'Thank you'; 'I love you'; and 'Good-bye'" are sufficient (Byock 1997, p. 140). For everyone, the chaplain has stressed the forgiving nature of God.

Chaplains can also enhance hope, help families understand how medicine can be a part of what they believe is ultimately God's healing role, and sustain them and their faith when physical healing is no longer possible. Many can provide comforting religious rituals such as meditation, prayer, sacraments, or the reading of sacred texts when the patient cannot participate in public religious services. They can also ascertain which rituals are important to those patients nearing the end of life and communicate these to the other staff working with the patient and family.

I encourage you to urge those of your patients who have good relationships with clergy to seek increased support from them. Even patients and families who do not consider themselves religious and who have no formal religious affiliation may find relief through expert pastoral counseling. They may receive guidance in their search for the meaning of their suffering. In this way, patients can often receive all the comfort and forgiveness they need and die at peace; in reply to the question "If you died tomorrow, would anything be left undone?" they could answer, "No" (Byock 1997).

Reevaluate When the Pain Pattern Changes

The final recommendation of the AHCPR guidelines is to assess each new pain. Pain assessment is an ongoing process, directed not only at determining the efficacy of the pain-relief regimen but also at detecting new pains so as to identify their causes. When the character, quality, or timing of the patient's pain changes, a new lesion is usually responsible. Disease may be advancing, a bone may have fractured, or a problem unrelated to the cancer may have developed. Frequent reassessment will detect these and enable us to institute effective therapy promptly.

Summary

A comprehensive pain assessment is the foundation of effective pain therapy and is not hard to accomplish. The guidelines from the AHCPR are straightforward, and validated measurement tools are available. When you broaden your focus so that the complaint of pain in your cancer patients is no longer simply a clue to the discovery of a reversible underlying cause, and you assess for the multiple causes and modifying factors discussed in this chapter, you are likely to gain a comprehensive understanding of your patients and their pain and to relieve their suffering.

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CHAPTER 6

Pharmacologic Management of Cancer Pain

Nonsteroidal Anti-inflammatory Drugs
- Using NSAIDs for Cancer Pain
- Selecting an NSAID
- Routes of Administration
- Side Effects
- Life-Threatening Toxicities

Opioid Analgesics
- General Guidelines for Opioid Use
- Selecting an Opioid Analgesic
- Routes of Administration

Preventing and Relieving Side Effects of Opioids
- Constipation
- Nausea
- Sedation
- Opioid Overdose
- Opioid Neurotoxicity
- Delirium
- Respiratory Depression
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- Summary

Adjuvant Analgesic Treatments
- Adjuvant Treatments for Neuropathic Pain
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Anesthetic Methods of Pain Relief
- Topical Anesthetics and Parenteral Lidocaine
- Local Anesthetics Taken Orally
- Neural Blockade and Neuroablation

Relieving Pain in Older Persons
Assessment
Management Considerations
Relieving Pain in Substance Abusers
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Patients on Methadone or Buprenorphine Maintenance
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Common Clinical Situations
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Rapidly Relieving Excruciating Pain
Summary
Tables
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Pharmacologic therapy is the mainstay of cancer pain relief. Satisfactory pain control for 90 percent of cancer patients can be achieved with minimal adverse side effects. But in 2012, a prospective, observational study of more than three thousand outpatients with breast, lung, colorectal, or prostate cancer found significant underprescribing of pain medications (Fisch et al. 2012). Two-thirds of these patients reported pain at their initial visit to their oncologist, and a month later, half of them (33 percent of the total) were receiving inadequate medications for their degree of pain. Patients who did not have advanced disease and who were not receiving antineoplastic therapy, and those who were treated at a center with a predominance of minority patients or who were minority patients treated at any center, were at particular risk for undertreatment. A full 43 percent of patients reporting severe pain were not receiving an opioid at their first assessment or a month later. Twenty percent were receiving no analgesic.

To achieve good pain control for your patients, you will need to be comfortable using a combination of oral, transmucosal, or transdermal opioid and adjuvant analgesics, along with other agents that prevent or treat opioid-induced constipation, nausea, sedation, and delirium. Only rarely will your patients need rectal, intravenous, subcutaneous, or spinal routes of opioid administration to achieve pain relief, and for these patients, I suggest that you collaborate with a palliative care colleague.

In this chapter I discuss the drugs you will need: non-opioid, opioid, and adjuvant analgesic medications, as well as other treatments, and agents that prevent or relieve opioid-induced side effects. I also review anesthetic methods that

can relieve pain. The special needs of older patients and substance abusers are included. I discuss some common clinical situations: how to start a patient on opioids; how to change opioid doses, routes, or agents; and how to relieve excruciating pain rapidly. This chapter's tables appear on pages 317–329.

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs), taken by people with mild to moderate nonmalignant pain, are useful alone or combined with an opioid for cancer patients with pain from various sources. They are especially useful for patients with bone pain or tissue inflammation.

The NSAIDs include the *p*-aminophenols (e.g., acetaminophen), the salicylates (e.g., aspirin and the nonacetylated salicylates such as salsalate), the propionic acid derivatives (e.g., ibuprofen), and the acetic acid derivatives (indomethacin, ketorolac) (see Table 6.1).

Most NSAIDs indirectly inhibit synthesis of prostaglandins. Prostaglandins synthesized as a consequence of injury to bones or joints help mediate the inflammatory response and the transmission of the pain signal. The majority of NSAIDs inhibit the synthesis or the function of both forms of cyclooxygenase (COX) enzymes required for the production of prostaglandins. COX-1 is present in the stomach, kidney, and blood vessels, whereas COX-2 is produced only in inflamed tissues. NSAIDs that inhibit COX-2 therefore minimize the inflammation associated with bone or tissue injury, whether a sports injury, arthritis, or a metastasis. NSAIDs that also inhibit COX-1, however, impair synthesis of the beneficial prostaglandins produced in the stomach and kidney and can therefore cause gastrointestinal distress and renal dysfunction.

Using NSAIDs for Cancer Pain

NSAIDs used alone usually do not provide sufficient relief for patients with cancer pain, though I have had some success with these drugs for patients receiving hormonal therapy for metastatic prostate cancer or aromatase inhibitors for breast cancer. When first prescribing an NSAID, generally start with the lowest effective dose and escalate to the maximum 24-hour dose (indicated in Table 6.1). Since both acetaminophen and aspirin have a ceiling effect (1000 mg is the ceiling dose for both agents), a patient gets no more pain relief from a 1500-mg dose of aspirin or acetaminophen than from a 1000-mg dose; he just gets increased

toxicity. If the initial agent chosen is ineffective at the maximal recommended dose or the patient develops an intolerable side effect, switch to one of the NSAIDs in a different chemical class (see Table 6.1).

Selecting an NSAID

To decide which NSAID to prescribe first, I consider the cause and intensity of the pain, any underlying illnesses that would contraindicate use of an NSAID, and the expected side effects. I also consider whether the patient can take oral medications or will need an intravenous or a rectal preparation.

PRACTICE POINTS: SELECTING AN NSAID FOR CANCER PAIN

- Review patients' underlying medical illnesses.
- Give NSAIDs alone for mild pain.
- Give indomethacin or ketorolac for pleuritic or pericardial pain and indomethacin for gout.
- Be aware of the "ceiling" effect: the maximum pain relief obtainable from acetaminophen or aspirin is from a 1000-mg dose.
- When pain is refractory to NSAIDs alone, add an opioid for mild to moderate pain.
- Ketorolac is effective for acute severe pain, especially for chest or feeding tube insertion; it should generally not be used for longer than 5 days at a time.

Knowing the cause of the pain and its intensity can sometimes help you choose the appropriate NSAID. Indomethacin or ketorolac, for example, are the drugs of choice for patients with pleuritic or pericardial pain, and indomethacin has special efficacy for gout. They often relieve the pain of these disorders rapidly and completely. Therefore, despite the risk of gastrointestinal and renal side effects and bleeding complications from these agents, I recommend them for these patients unless they have a coagulation problem or known renal or ulcer disease.

Underlying illnesses also help direct the choice of NSAID. All NSAIDs should be avoided in patients with a known allergy to aspirin or with asthma, as they can produce bronchospasm in up to 20 percent of these patients. Patients at high risk for complications include those over age 60 (those over 70 are at an even

higher risk) and those with a history of previous ulcer disease, NSAID-induced bleeding, or cardiovascular disease. These risks are additive. Other risk factors include concomitant use of corticosteroids or anticoagulants and use of multiple NSAIDs. To minimize gastrointestinal ulcers and bleeding frequency, high-risk patients should be started on COX-2 selective agents rather than nonselective NSAIDs (Chan et al. 2002, Laine 2003). The risk is so high for patients taking anticoagulants that they should never take an NSAID that inhibits prostaglandin synthesis.

Patients who have somatic or inflammatory pain but who also have moderately reduced platelet counts (<100,000/mm^3) or inherited coagulation disorders (such as hemophilia) can take the COX-2 selective agent celecoxib (Celebrex) or an NSAID that does not affect cyclooxygenase or prostaglandin synthesis, such as choline magnesium salicylate or salsalate, and not have an increased risk of bleeding (Reynolds et al. 2003). Patients taking anticoagulants such as warfarin, however, cannot take celecoxib. The interaction in the metabolism of warfarin and celcoxib causes marked increases in the INR and an increased risk of bleeding. Two other COX-2 selective agents, valdecoxib (Bextra) and rofecoxib (Vioxx), were voluntarily withdrawn from the market because of side effects and cardiovascular safety concerns.

Patients with congestive heart failure, cirrhosis, or chronic renal failure experience increased edema, worsening renal function, or hypertension if treated with either nonselective agents or COX-2 inhibitors, so both should be avoided (DeMaria and Weir 2003).

For patients with mild to moderate somatic or visceral cancer pain refractory to NSAIDs alone, aspirin and acetaminophen are effective when combined with an opioid. The most commonly used combination pills contain 5 mg of oxycodone along with either 325 mg of aspirin (e.g., Percodan), 325 mg of acetaminophen (e.g., Percocet), or 500 mg of acetaminophen (e.g., Tylox). Unfortunately, patients can take only a limited number of these pills each day because of the toxicities of the acetaminophen and aspirin. Patients who need more opioid can take higher doses of an oxycodone or other opioid preparation along with a safe dose of an NSAID. A patient with uncontrolled bone pain from metastatic breast cancer, for example, might be switched safely from twelve oxycodone/acetaminophen tablets a day, which contain 60 mg of oxycodone (5 mg × 12 pills = 60 mg), to 30 mg of sustained-release oxycodone every 12 hours along with acetaminophen 1000 mg orally every 8 hours.

Ketorolac (e.g., Toradol) is likely to be effective for someone with acute, severe somatic or inflammatory pain, such as someone with a chest tube or a g-tube,

or one of the conditions listed above. Because ketorolac has the pain-relieving potency of an opioid, it is also used in situations in which the clinician does not want to prescribe an opioid but the patient needs the level of pain relief an opioid can deliver. For example, ketorolac is frequently given by emergency room physicians who wish to avoid the mental status changes that opioids can induce. In this setting, it is given parenterally (see Table 6.1 for doses and frequency). A 30-mg dose of parenteral ketorolac is equivalent in pain-relieving potency to 15 mg of parenteral morphine. However, ketorolac can impair renal function and is therefore contraindicated for patients with renal insufficiency. And it cannot be used for chronic pain relief because it is associated with a significant incidence of acute renal failure and gastrointestinal side effects. A typical course of ketorolac is limited to five days of up to 4 doses per day every 6 hours standing or as-needed IV (it is not effective orally), combined with a proton pump inhibitor.

Routes of Administration

For patients who cannot take oral preparations, aspirin, indomethacin, and acetaminophen can be given rectally (Samala and Davis 2012) and are available by suppository. Suppositories should be inserted base first, to promote retention. Though available only as a liquid, naproxen may be the best choice because it has the longest half-life and 80 percent bioavailability. Ten to 30 ml of the liquid suspension (125 mg / 5 ml) can be given twice a day. Ibuprofen is not available in suppository form, and the liquid suspensions are available only in pediatric doses (100 mg / 5 ml). A therapeutic dose of ibuprofen would necessitate giving 30 ml rectally (p.r.) every 4 to 6 hours, and this may be difficult for patients to tolerate.

Side Effects

The inhibition of prostaglandin synthesis can cause several serious abnormalities in platelet and kidney function, as well as in the lungs and the gastrointestinal tract. Because prostaglandins are necessary for normal platelet function, most NSAIDs impair platelet function and predispose the patient to bleeding. And since prostaglandins are also required to maintain renal arterial blood flow, NSAIDs may precipitate renal failure in patients with impaired flow, such as many elderly patients. NSAIDs may also enhance salt and water retention and cause edema to develop in patients with congestive heart failure or cirrhosis.

PRACTICE POINTS: TOXICITY OF NSAIDS

- Avoid NSAIDs for patients older than 70 and for those with thrombocytopenia, coagulation defects, renal failure, cirrhosis, heart failure, or asthma.
- Use nonacetylated salicylates (e.g., choline magnesium salicylate or salsalate) for patients taking anticoagulants or with thrombocytopenia or bleeding disorders.
- Consider adding a proton pump inhibitor (e.g., esomeprazole) to prevent gastrointestinal ulceration for patients older than 60 or for those with a history of peptic ulcer disease.
- Avoid NSAID/oxycodone or acetaminophen/oxycodone combinations. Rule out salicylate toxicity in a patient taking a combination agent who develops otherwise unexplained mental status changes, ataxia, or tachypnea, even if there are no complaints of tinnitus.

Life-Threatening Toxicities

The side effects described above occur with therapeutic doses of NSAIDs. At toxic blood levels, however, some of the NSAIDs can be life-threatening.

Aspirin overdose. Aspirin can be particularly dangerous. Aspirin and the nonacetylated salicylates are metabolized by the liver; less than 5 percent is excreted by the kidneys. But the liver can metabolize only a limited amount of aspirin; if a person ingests more than that, the drug accumulates and can rapidly reach toxic levels. Patients who increase their dose of aspirin much above 6000 mg/day can easily develop salicylate toxicity, which manifests as tinnitus, ataxia, hyperventilation, delirium, and even coma.

Few patients would knowingly take that much aspirin, but aspirin can be "hidden" in the combination products mentioned above. It's not hard to imagine that someone could have an exacerbation of her pain, double or triple the amount of Percodan she is taking, and, in consequence, develop an aspirin overdose. Older patients with presbycusis may be at particular risk because they cannot hear tinnitus. Despite my warnings to the contrary, a number of patients have increased their aspirin intake in this way and developed life-threatening salicylism.

The "Drunk" with an Undetectable Alcohol Level

Mr. Lafferty was one such patient. He was taking two Percodan every 4 hours for his metastatic prostate cancer pain. His wife called to ask our advice because, she said, *"He is staggering around and talking out of his head like he used to when he was*

drunk all the time. But when I took him to the local emergency room, they said he couldn't be drunk; there was no alcohol in his blood."

As it turned out, her husband had not been drinking. When she inspected his medication bottle, she found that instead of the 12 pills a day he normally took, he had taken 25 Percodan the day before. These contained 8125 mg of aspirin! I asked her to take Mr. Lafferty back to the hospital because he needed immediate medical attention.

When he again arrived in the emergency room, the triage nurse noted that he was still ataxic and confused, and I could understand why she thought he was inebriated. On further evaluation, he was also found to be hyperventilating because of the metabolic acidosis the salicylate induces. An electrolyte panel confirmed the characteristic anion gap acidosis. To minimize the deposition of salicylates in his central nervous system (CNS) and to increase salicylate clearance, the emergency medical staff gave him intravenous sodium bicarbonate. They also avoided any agents that could sedate him, because if he stopped hyperventilating, the acidosis would worsen, more aspirin would deposit in his CNS, and he would deteriorate further. Mr. Lafferty responded well to this therapy and was back to his old self within a few days.

Acetaminophen overdose. Aspirin toxicity is not uncommon, but it would be very difficult for a patient with normal hepatic function to accidentally take enough acetaminophen to induce serious toxicity. This would require an intake of more than 20 g of acetaminophen at one sitting. Even someone taking a combination preparation of acetaminophen and oxycodone containing 500 mg of acetaminophen per pill would have to take 40 tablets over 1 to 2 hours.

In patients who have chronic liver disease, however, such as that induced by alcohol, liver toxicity can develop even with therapeutic acetaminophen doses, and accidental overdose may occur. If you discover such an overdose soon after the patient ingests the acetaminophen, you can prevent hepatic toxicity with Mucomyst. But if the overdose is recognized late, Mucomyst will be ineffective. Liver transplantation can be life saving for appropriate patients.

Opioid Analgesics

Although NSAIDs can be useful, opioids are necessary for the vast majority of cancer patients with pain. Obtaining the appropriate opioid is much easier than it was a decade ago. State Cancer Pain Initiatives, which now exist in all fifty states, worked to induce legislators to remove the legal barriers to prescribing

opioids for cancer patients. The Medical Board of California, for example, adopted guidelines for intractable pain in 1994, which it republished in 1996. It states in the 1996 introduction,

> The under treatment of intractable pain is often a more significant problem than over treatment, and one reason among many is the physician's fear that a complaint for over prescribing may put his/her license in jeopardy. The Medical Board of California (MBC) is aware of this dilemma and encourages physicians to apply their best medical judgment when treating the patient, rather than basing their treatment on a fear of discipline by the MBC . . . The MBC created these requirements to complement legislation . . . which established California public policy as supportive of the responsible practice of pain management. Simply stated, the treatment of chronic pain, as is true with any medical treatment, must be consistent with established medical standards that serve the patient's total well-being. These guidelines are being republished to reinforce the MBC's position that the public is best served by a health care environment where physicians are free to exert their own best medical judgment consistent with accepted community standards of care.

In addition, the Medical Board of California requires that all licensed physicians show proof of six hours of CME in pain management and an additional six hours in end-of-life care.

As the third edition of this work is being prepared, prescription drug abuse is posing the latest threat to the ability of cancer patients to receive the opioids they need. As state legislators try to protect their citizens from the dangers of opioid overdose, they enact new requirements that create extra hurdles for clinicians. It remains to be seen if and how these regulations will affect the care of cancer patients.

Drugs like Embeda, however, offer a creative solution to the problem of drug abusers crushing extended-release tablets to get the high from the larger dose of opioid released from the tablet. Embeda contains both extended-release morphine and the opioid antagonist naltrexone. The naltrexone, however, is sequestered in a core and is not released unless the pill is crushed, which is not the way it is intended to be used. If the pill is crushed, the naltrexone prevents the user from getting high from the morphine.

Availability and cost, once barriers to obtaining effective opioids, have become less of a problem (see Table 6.2). Increasing numbers of community pharmacies, particularly those that work with home hospice agencies, now carry

even potent opioids in stock or will obtain them within 24 hours of receiving the prescription. Difficulties remain, however, for minority patients living in areas in which minorities make up the majority of the population (Morrison et al. 2000). For patients receiving the Medicare Hospice Benefit, all drugs that provide comfort care, including opioids, adjuvant agents, and agents that treat side effects, are covered. And for patients with limited financial means, there is an effective and inexpensive opioid: methadone.

General Guidelines for Opioid Use

Pharmaceutical companies have provided numerous agents in a variety of formulations, and now we can largely tailor the drug to the patient's needs. Uncontrolled pain, however, remains one of the major obstacles to cancer patients accomplishing their goals. Some of the reasons for this are inadequate pain assessment, physicians' reluctance to prescribe opioids in the appropriate frequency and dose, and patients' reluctance to take them. Physicians also may mistakenly believe that for patients taking opioids, the medication will interfere with the ability to diagnose the cause of acute pain in the emergency setting. In fact, in a prospective, randomized trial, patients arriving at an emergency room with abdominal pain of unknown etiology were initially (i.e., for the first 60 minutes) given morphine or saline. This study found no occasions when the administration of morphine masked a physical finding or led to a decrease in diagnostic accuracy (Thomas et al. 2003).

Adhering to the following guidelines may help.

Guidelines for Opioid Use

- Give "whatever it takes" to relieve the patient's pain; be sure that the opioid dose is adequate.
- Give opioids often enough to prevent the pain from recurring.
- Use the least invasive route.
- Use adjuvant medications to minimize opioid-induced side effects.

What is an "adequate dose?" An adequate opioid dose is whatever dose is needed to provide pain relief, no matter how high. There is no arbitrary "maximal dose" of any opioid (except for meperidine). But the higher doses often cause neurotoxicity, and it's usually better to change the patient's medication to a different, more potent agent. For example, if a patient receiving 20 mg/hr of intravenous morphine along with appropriate adjuvant medications still has pain, even though he does not have unacceptable side effects now, he would be

likely to develop them as you increase the dose. Most patients who need these very high doses have neuropathic pain and therefore would benefit from a rotation to methadone. Later in this chapter, I review why this is so and how to do the rotation.

Scheduling of doses. Many patients with advanced cancer whose pain rarely remits should be taking the drugs at regularly scheduled intervals around the clock rather than as needed (p.r.n.). They need both a long-acting agent or sustained-release formulation of an opioid to relieve their baseline, steady pain and a short-acting opioid to relieve unexpected exacerbations. Doses of a short- or immediate-acting preparation given to someone who is taking around-the-clock opioids are often referred to as rescue doses: they rescue the patient from breakthrough pain. With the variety of available agents, around-the-clock pain control is usually achievable.

Mild to moderate cancer pain may be intermittent, however, and for patients with this kind of pain, p.r.n. dosing may be appropriate. When they are at home, they can give themselves pain medicine whenever they need it. But hospitalized patients can experience significant delays in receiving needed p.r.n. medication. For these patients, instead of ordering opioids "p.r.n.," I use a "patient-may-refuse" order. The nurse offers the medication regularly (e.g., oxycodone every 4 hours), and the patient has the option to take it or refuse it.

Use the least invasive route. Ninety percent of cancer patients will be able to take opioids orally, transmucosally, or apply them transdermally in a skin patch. The drugs can also be given rectally. Even patients who are dying will seldom need intravenous, intramuscular, subcutaneous, or intraspinal opioids.

Use adjuvant medications. More opioid will *always* provide more pain relief, but the higher doses will also cause more side effects. Dr. Michael Levy, one of the leaders in pain management in the United States, has extended the concept of the therapeutic window to enable us to more easily conceptualize the balance between pain relief and opioid-induced side effects (Levy 1996). The *therapeutic window* of any drug is the range of blood concentrations in which it is effective but not toxic. What Dr. Levy points out is that different patients may have very different therapeutic windows even for the same opioid.

In patients who have normal renal and hepatic function and whose pain is of somatic or visceral origin, the window may be wide open; that is, they can take the amount of opioid they need with minimal, easily controllable side effects. But in other patients, those with renal, hepatic, or mental impairment or with neuropathic pain, that window may be all but closed. The patient may experience intolerable side effects without being able to achieve satisfactory pain relief.

Dr. Levy suggests we first try to "widen the window" by treating any underlying conditions that would exacerbate an opioid-induced side effect. To minimize sedation, for example, aggressively treat hepatic encephalopathy. But for patients in whom (to extend the metaphor) the window is stuck, add non-opioids as adjuvant agents to minimize the opioid dose needed for effective pain relief.

Because adjuvants cause their own side effects, add them only when a patient cannot achieve satisfactory pain relief without them. Don't use them simply to lower the opioid dose in a patient whose pain is well controlled with opioids with minimal side effects.

Selecting an Opioid Analgesic

Patient preference. For my initial choice of drug, I consider patients' preferences, which are influenced by their past experiences with opioids. For example, a patient who has had his wisdom teeth extracted might have had good pain relief from short-acting combinations of oxycodone and aspirin or acetaminophen. If he now needs something more long acting, I can use that same opioid (oxycodone) in a sustained-release preparation.

If, on the other hand, the patient had a serious side effect from an opioid, I know to avoid that agent and, if possible, other agents in the same class. Unfortunately, except for transmucosal fentanyl, all the immediate-acting potent opioids are structurally related to morphine. Unless the patient has had a true morphine allergy, you will usually be able to switch to another opioid that is less likely to cause the troublesome side effect. If, for example, a patient has nightmares or hallucinations from morphine, you can switch her to an equianalgesic dose of hydromorphone. The rare patient with a true morphine allergy can take transmucosal fentanyl (if opioid tolerant) or methadone, neither of which is chemically related to morphine.

Pain intensity. Next, determine the pain's intensity. As I discussed in Chapter 5, pain intensity can be measured using various numerical, word, face, or behavioral scales. In a numerical rating scale, pain ratings of 1 to 4 are considered mild, 5 to 6 moderate, and 7 to 10 severe. The World Health Organization (WHO) has adopted an "analgesic ladder" based on these ratings (Figure 6.1) and guidelines for using it to relieve cancer pain.

In addition to these guidelines, WHO recommends a stepwise escalation that matches the potency of the opioids to the intensity of the pain. For mild pain, start with non-opioid analgesics. Moderate pain should be treated with less potent step 2 agents or low doses of potent opioids (see Table 6.3), and severe pain

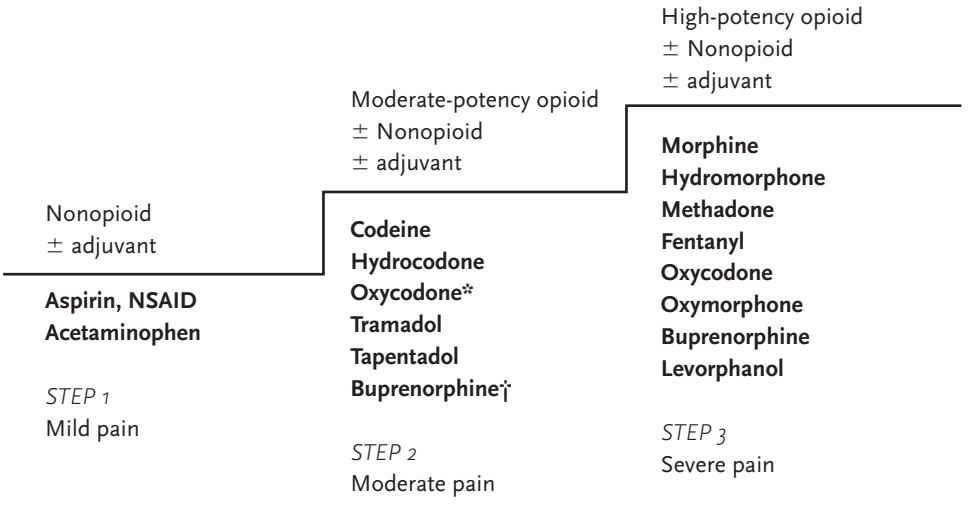

Figure 6.1. Analgesic ladder. *Oxycodone (5–10 mg) in combination with aspirin, acetaminophen, or NSAID is a step 2 agent; alone, it is a step 3 agent. †At dose levels available in the United States (as of 2013), buprenorphine is a step 2 agent. Adapted from the World Health Organization, *Cancer Pain Relief: With a Guide to Opioid Availability*, 2nd ed., Geneva: World Health Organization, 1996.

with the most potent step 3 opioids (see Table 6.4). Non-opioid analgesics and adjuvant medications should be added at any step when indicated.

In addition, if a patient has pain that is unrelieved by the agents recommended for that step, the WHO guidelines suggest moving up to the next step. If a patient with mild to moderate pain, for example, does not get adequate pain relief from a step 2 agent, a step 3 opioid should be prescribed. The WHO ladder and guidelines have been shown to be very effective, even in dying patients. In one study in which they were used, at the time of death, only 3 percent of patients reported severe pain, and no patient died of respiratory depression due to the opioids (Mercadante 1999).

Step 2 agents. In my experience, cancer pain is rarely, if ever, mild. For cancer patients with mild to moderate pain, I have found low-dose hydrocodone/acetaminophen combinations (e.g., Vicodin, Lortab) and codeine to be the *least* useful of the step 2 opioids. The dose of hydrocodone in the Vicodin or Vicodin ES preparations is not strong enough, and codeine is often nauseating and causes dysphoria. A higher-dose hydrocodone is available in a combination preparation, Vicodin HP CIII, which contains 10 mg of hydrocodone with 660 mg of acetaminophen per tablet; this should be given orally every 4 hours. There is no parenteral preparation. (See Table 6.3.)

PRACTICE POINTS: SELECTING AN OPIOID

- Consider patient preference when choosing the opioid and the opioid formulation.
- Match opioid agent with pain intensity using the WHO ladder; advance up the ladder if pain persists, even if the patient still characterizes it as "mild" or "moderate."
- Match opioid formulation to the temporal pattern of pain (i.e., continuous, intermittent, or both).
- Except for patients who have previously used codeine with good results, avoid codeine for cancer patients.
- Consider methadone for patients with severe neuropathic pain, or when drug cost is important.

Codeine. Codeine is problematic in cancer patients, for several reasons. Although the side effects of codeine may be helpful in discouraging abuse in people with nonmalignant pain, these effects are unacceptable in someone with cancer pain. Further, for codeine to provide pain relief, it must be metabolically converted to morphine by a specific hepatic enzyme. Patients who either lack that enzyme or are taking drugs such as cimetidine that inhibit the enzyme's function will get little or no analgesia from codeine.

Oxycodone. Oxycodone (at low doses), tramadol, and tapentadol are effective step 2 agents for cancer patients. Oxycodone is a useful oral opioid analgesic for patients with mild to moderate cancer pain. It is listed with both the step 2 and step 3 agents because in step 2, several formulations combine a low dose (5 to 10 mg) of oxycodone with an NSAID. All provide excellent relief for this degree of pain, often induce slight euphoria, but cause only mild to moderate constipation. Many patients with moderate, intermittent pain due to bony metastases from breast, lung, or prostate cancer respond very well to these agents. For unclear reasons, women have a 25 percent higher blood level of oxycodone than men after ingesting the same dose (Kaiko, Benziger et al. 1996). To minimize side effects, consider using lower initial oxycodone doses for female patients.

Tramadol. Tramadol (e.g., Ultram) is also useful for cancer patients with mild to moderate pain. It is a centrally acting, non-opioid analgesic that is chemically unrelated to opioids but binds to one of the opiate receptors. Approximately one-third of its analgesic effect is reversed by naloxone. The rest of the analgesia it produces may be due to its ability to decrease reuptake of norepinephrine and serotonin.

Tramadol can relieve mild to moderate somatic or neuropathic pain, including post-herpetic neuralgia (Gobel and Stadler 1995); 100 mg of tramadol is more effective than 60 mg of codeine but is approximately equivalent in potency to 60 mg of codeine plus 650 mg of acetaminophen or aspirin. Side effects are similar to those caused by opioids, but in addition, tramadol may increase the risk of seizures in certain patients. Tramadol may also precipitate a serotonin syndrome in patients already taking SSRIs (Mahlberg et al. 2004).

The usual dosage is 50 to 100 mg every 4 to 6 hours; total 24-hour dose should not exceed 400 mg. Doses should not exceed 300 mg for patients over 75, or 200 mg for patients with renal insufficiency or cirrhosis. Tramadol is available in Europe in a once-daily formulation that provides pain relief equivalent to that of standard-release capsules taken three times a day (Bodalia et al. 2003).

Tapentadol. Tapentadol is an oral, centrally acting analgesic that both binds mu opiate receptors and inhibits the reuptake of norepinephrine (Wade and Spruill 2009). As such, it is of particular efficacy for patients with neuropathic pain. It has not been studied in patients with cancer pain but has been studied in several phase III trials (Wade and Spruill 2009). Patients receiving 50 or 100 mg of tapentadol (q4h-6) for chronic osteoarthritis pain had about the same relief as those receiving 10 to 15 mg of oxycodone, but had less nausea, vomiting, or constipation. No dose adjustments are needed for mild to moderate renal or hepatic impairment. However, tapentadol must be used with caution along with SSRIs and SNRIs, tricyclic antidepressants, MAO inhibitors, or other agents that impair serotonin metabolism, because serotonin syndrome can result.

Step 3 opioid agents. For patients with more severe pain, the potent step 3 opioids are needed (see Table 6.4). Opioids in the morphine "family" include, besides morphine, hydromorphone (e.g., Dilaudid), oxymorphone (e.g., Opana), oxycodone, and levorphanol (e.g., Levo-Dromoran). The other step 3 opioids, methadone, meperidine, and fentanyl, are not structurally related to morphine. Any of these can be safely used for patients with normal renal and hepatic function. All are metabolized by the liver and renally excreted. These opioids should all be used with caution and at lower doses in patients with hepatic failure.

Morphine has an active metabolite, morphine-6-glucuronide (M-6-G), which is excreted by the kidney. If the creatinine clearance decreases by half, doses of opioids in the morphine family of agents should be reduced or their frequency of administration changed accordingly. Meperidine should not be given to patients with renal insufficiency because the half-life of its active metabolite, normeperidine, prolongs in renal failure and causes severe toxicity. Methadone and fentanyl may be used safely in patients with renal failure or who are on dialysis.

Oxymorphone. Parenteral oxymorphone (e.g., Numorphan) has been used for many years for pain relief. More recently, both immediate (e.g., Opana) and sustained-release oral forms (e.g., OpanaER) have become available in the United States (Craig 2010; Sloan 2008). Oral oxymorphone is about twice as potent as oral oxycodone. The recommended starting dose of immediate-release oxymorphone for an opioid-naive patient with acute, moderate to severe pain is 10 mg every 4 to 6 hours; 5 mg of the sustained-release form can be started every 12 hours.

Methadone. Methadone is not a new drug, but it is being increasingly used for patients with moderate to severe pain. It is by far the least expensive of the opioids and has particular utility for patients with neuropathic pain—the most refractory type of pain.

Methadone is structurally unrelated to the morphine family of drugs and to meperidine and fentanyl, and it can be used in the rare case of true allergy to these agents. It is available in oral, subcutaneous, intravenous, and rectal formulations. If you are giving methadone by the intravenous or subcutaneous route, use half the oral dose. Topical preparations of methadone, however (10 to 45 mg/day as a powder dissolved in PLO [pluronic lecithin organogel]), are not effective: the levels that are reached are inadequate to provide analgesia (Sylvester et al. 2011). Subcutaneous infusions are problematic because methadone causes local irritation, and the inflammation can interfere with the absorption of the drug. Rotate the infusion site every few days, or use intermittent boluses rather than infusions; add dexamethasone, which extends the use of the site for a continuous infusion up to 5 days; bolus doses or infusions of hyaluronidase may also help (Shaiova et al. 2008).

Methadone is particularly useful for patients, usually with severe neuropathic pain, who are suffering from the neurotoxic side effects of the high doses of other opioids that are often needed to control that type of pain. Now that I have become comfortable using it, I use methadone as the initial opioid for patients with moderate to severe neuropathic pain. In elderly patients suffering from vascular insufficiency pain, which is a type of neuropathic pain, doses as low as 1 to 2 mg two to three times a day have been very effective and cause minimal side effects.

Why is methadone particularly helpful in treating neuropathic pain? Methadone contains d- and l-isomers that act as opioid receptor agonists and NMDA (*N*-methyl-d-aspartate) receptor antagonists (Knotkova et al. 2009). Patients with neuropathic pain and patients taking opioids over the long term have increased levels of NMDA receptors in the dorsal horn of the spinal cord. NMDA

antagonizes the activity of the opiate receptors, so blocking the NMDA receptors enhances the analgesic effect of externally administered opioids. Methadone also inhibits the reuptake of serotonin and norepinephrine (Moryl et al. 2008).

Methadone can be given to patients in renal failure because it has no known active metabolites and does not accumulate. The difficulties with using it lie in its biphasic elimination, its metabolism by CYP 3A4 isoenzyme (one of the isoforms of the cytochrome P450 system), its effect on the QTc interval, and its controversial equianalgesic dosing range.

Because of methadone's initial distribution phase, if you are using it as the only opioid, the first loading usually requires that it be given every 4 to 6 hours (Shaiova et al. 2008). But methadone has a second, extended phase lasting 36 to 60 hours, which causes drug levels to accumulate. By the fifth to sixth day of treatment, methadone usually needs to be taken only twice to three times a day to maintain analgesia and only once a day to prevent withdrawal. After the first few days of methadone therapy, therefore, the dosing interval should be increased to two or three times a day to minimize the chance of inducing sedation or respiratory depression. Alternatively, you can give the methadone three times a day from the start, and use rescue opioids for a day or two until the methadone serum levels rise. If the rescue doses are effective, this is what I do, because it is less likely to lead to oversedation or respiratory depression in the second or third day of methadone therapy. (I discuss below how to rotate patients from another opioid to methadone.)

Methadone interacts with inducers and inhibitors of the cytochrome P450 system. Patients must be monitored when methadone and a drug that is also metabolized by CYP1A2, CYP3A4, and CYP2D6 are given together; CYP1A2 and CYP3A4 are induced by a number of drugs and other substances (e.g., cigarette smoke), and CYP2D6 has a genetic polymorphism. Once you stabilize patients on methadone, I'd suggest that you check for methadone drug interactions on a website (such as www.drugs.com/drug-interactions/methadone.html) every time you start or discontinue one of their drugs. Drug levels can increase; methadone levels can increase or decrease; and there's no way to be sure unless you check.

When patients are receiving methadone, drug levels of desipramine (or other tricyclic antidepressants) and zidovudine increase. Drugs that lower the levels of methadone include antiretrovirals, phenytoin (by 50 percent), phenobarbital, carbamazepine, rifampin, somatostatin, spironolactone, and risperidone, each of which has precipitated withdrawal symptoms (Bruera and Sweeney 2002). Drugs that raise the serum methadone levels and that are commonly used in patients who have cancer include fluconazole, voriconazole, fluoxetine,

and fluvoxamine. The selective serotonin reuptake inhibitors (SSRIs) may raise methadone levels in CYP2D6 rapid metabolizers (Tarumi et al. 2002). The serotonin norepinephrine reuptake inhibitors (SNRIs; e.g., venlafaxine) do not. Grapefruit juice and acute alcohol use can increase methadone levels; chronic alcohol use may decrease them.

Methadone also prolongs the QTc interval, and patients who at baseline have a prolonged QTc interval, or who need high doses of methadone, have developed cardiac arrhythmias (torsades de points; polymorphic ventricular tachycardia) and even death as a result. Most of the reports of cardiac arrhythmia were in patients on a methadone maintenance program taking more than 300 mg a day; the cancer patients who developed problems were taking more than 600 mg of methadone per day.

Many patients don't require that high a dose of oral methadone. What is their risk? Reddy and colleagues (2010) prospectively measured the QTc intervals of cancer patients at 2, 4, and 8 weeks after patients began taking methadone. Twenty-eight percent of their patients had a prolonged QTc interval at baseline, due mainly to reversible conditions such as medications (found in 75 percent), or more rarely, hypokalemia or hypocalcemia, though 25 percent had structural cardiac disease. The patients with a baseline QTc interval prolongation had a much greater chance of worsening the QTc than patients without initial QTc interval prolongation, but only 1 of the 28 patients developed a QTc of greater than 500 (it was 509), and that patient's baseline QTc interval was 498 msec.

At the 8-week point, the median QTc was 373, and the median dose of methadone was 28 mg per day; the doses of methadone never exceeded 100 mg per day, and no other patients developed a QTc greater than 500 msec. These findings suggest that with low-dose methadone (<100 mg/day), even in patients with underlying QTc interval prolongation, significant QTc prolongation does not occur. What monitoring schedule is needed for cancer patients receiving more than 100 mg methadone per day, who are not placed on other agents that prolong the QTc interval, is not clear (Gourevich 2009). Every effort should be made to avoid hypocalcemia and hypokalemia, of course.

Methadone must be used with caution, or the QTc interval monitored, however, if the methadone is given intravenously or drugs are added that also prolong the QTc interval. Intravenous methadone is stabilized with a preservative (chlorobutanol) that blocks potassium channels. If your patient develops a prolonged QTc interval when switched from oral to intravenous methadone, use the preservative-free methadone if it is available in your site (Shaiova et al. 2008). Common drugs used in patients with cancer that prolong the QTc interval include the quinolone antibiotics (especially levoquin), typical and atypical

antipsychotics (such as haloperidol and olanzapine), SSRIs (but not SNRIs), metoclopramide, and certain chemotherapy agents like epidermal growth factor receptor inhibitors and tamoxifen.

Other difficulties with using methadone lie in the controversy about its equianalgesic dosing range (Knotkova et al. 2009; Moryl et al. 2008). Some studies have reported that the equianalgesic dose of morphine to methadone varies as the dose of morphine increases (Knotkova et al. 2009). Dose ratios vary from 4:1 at morphine doses of 30 to 90 mg, to 6:1 at 90 to 300, and to 8:1 at doses of more than 300 mg of morphine. Other studies report a ratio of 20:1 for doses of oral morphine equivalents greater than 1000 mg.

Why do we need relatively so much less methadone for patients on higher doses of opioids? I'm not sure, but the way I think about it, patients taking high opioid doses have a large amount of pathologic destruction of their nerves (such as cancer patients with plexopathies). The constant firing of those damaged nerves may lead their spinal cords to generate the greater number of NMDA receptors we know these patients have. And we know that NMDA receptors inhibit the ability of opioids to prevent transmission of the pain signal. When we give the patient methadone, we do two things: the d-isomer of methadone (which is 50 percent of the drug we give the patient) inactivates the inhibitory activity of the NMDA receptors (Knotkova et al. 2009), leaving the opioid receptors able once again to be inhibited by opioids, and the l-isomer binds the opioid receptors. So we need much less methadone than we would expect.

Conversion to Methadone. I usually take three days to convert my patients to methadone, because it is going to take at least three days for the dose of methadone I give the patient on day one to reach a steady state (i.e., after 3 half-lives). There will be higher blood levels of methadone on day two than day one, and even higher levels on day three. I usually need to make the change in a patient with unrelieved neuropathic pain who is taking a great deal of short-acting rescue opioid, because the sustained-release opioid or the intravenous continuous infusion is not working. The rescue doses work, but only for a short time, and the amount of drug needed is often causing myoclonus or other opioid neurotoxicities.

My goal is to load the patient slowly and safely with methadone, leaving the other opioids in place just long enough for the methadone levels to finally relieve the pain. I don't want to stop the "basal" opioids (sustained-release tablets or opioid continuous infusion) too soon, because the patient would be in more pain, relying solely on rescue dosing. In most cases, patients need less and less rescue medication each day as the methadone levels rise. I am able to taper off the old basal opioid over several days, so that by day three or four, patients are taking

methadone as the new "basal" medication, along with p.r.n. doses of short-acting rescue medications.

I did this for Josh, a 31-year-old fireman who had a refractory, recurrent sarcoma in his pelvis. He had severe neuropathic pain that was not responding to sustained-release oxycodone. Josh did not want to come into the hospital to have his pain more quickly controlled. His partner, Sam, however, was a nurse, and Sam promised to keep good records of all the medications Josh took, and to call daily to let me know their effect and any side effects. If Josh didn't have such a reliable and knowledgeable home caregiver, I would have insisted he be admitted to bring his pain under better control as we rotated him to methadone.

To calculate what dose of methadone to start with, I used the morphine:-methadone ratios shown in the box below, along with a hefty fudge factor to be conservative. Josh was taking 200 mg of sustained-release (SR) oxycodone every 8 hours (i.e., 600 mg/day), and he had taken an additional 300 mg in oxycodone rescue doses each day for the past several days (i.e., 5 doses of 60 mg each). I planned to convert only the sustained-release oxycodone to methadone.

Step 1. Calculate the equianalgesic dose of oral morphine.
600 mg of oxycodone (200 mg × 3 doses) = 900 mg of oral morphine (20 mg of oxycodone = 30 mg of oral morphine).
Step 2. Identify the correct morphine:methadone ratio
The ratio to choose for 900 mg of oral morphine is 15 of oral morphine to 1 mg of oral methadone.
Step 3. Calculate the 24-hour methadone dose.
900 / 15 = 60 mg.
Step 4. Be conservative, and cut the calculated dose in half.
30 mg of methadone per day, or 10 mg p.o. t.i.d.

As Dr. Russell Portenoy* pointed out to me a long time ago, because of the way the ratios work, after all the calculations, you usually end up with 5 mg p.o. t.i.d. or 10 mg p.o. t.i.d. of methadone as a starting dose. That's certainly been my experience and that of my team.

DAY 1. Josh's pain level is 10/10 and not acceptable.

Recommendation: 200 mg SR oxycodone every 8 hours, along with 10 mg of oral methadone every 8 hours and whatever rescue doses of

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60 mg oxycodone every 4 hours he needs (he had the oral liquid concentrate of oxycodone at 20 mg/ml).

DAY 2. Josh needed only two rescues doses, each early in the previous day, and Sam said that he had slept through the night. His pain level is 6/10 and not acceptable.

Recommendation: Decrease SR oxycodone to 100 mg every 8 hours; continue the 10 mg of methadone every 8 hours and the rescue opioid dose of 60 mg oxycodone every 4 hours as needed.

DAY 3. Josh again used only two or three rescue doses; his pain level is now 5/10 and acceptable.

Recommendation: Stop all SR oxycodone and continue only the t.i.d methadone and immediate-release oxycodone p.r.n.

DAY 4. Josh's pain level is 4/10 and acceptable without any excessive sedation. He needed only two doses of prn oxycodone the day before. Josh has therefore been effectively and safely converted to oral methadone, with oral oxycodone for rescue.

If Your Starting Dose Is Too High. If on day two, Josh's pain level had been a 3 and acceptable, I would have realized that the dose of methadone was too high for him, and that if I continued it, he would be asleep and possibly even have respiratory depression by day three. I would therefore have decreased the SR oxycodone by 50 percent, and decreased the methadone to 10 mg p.o. twice a day.

If Your Starting Dose Is Too Low. If Josh had needed 300 mg rescue oxycodone on day one, I wouldn't have decreased his SR dose day two, but would have continued to monitor the as-needed usage. I don't decrease the SR opioid until there is a significant decrease in the use of p.r.n. opioid. If Josh had still had 8/10 pain on day three and was taking significant rescue doses, I would have increased his oral methadone dose to 15 mg every 8 hours and continued to monitor his pain levels and use of rescue medications.

When you first do these opioid rotations to methadone, it's wise to work with someone who has experience using the drug, such as an anesthesia pain or palliative care colleague, a hospice medical director, or a clinical pharmacist who works with a hospice team. They can check your calculations, offer cautions about drugs the patient is on that can increase or decrease methadone levels, or the QTc interval, and help you know when to increase or decrease the methadone dose and the patient's other opioids.

The danger of meperidine/normeperidine. You are probably wondering why meperidine (Demerol) is not included in the lists of step 2 and step 3 agents. Meperidine is useful for postoperative and postpartum pain or to relieve a vari-

PRACTICE POINTS: WHY MEPERIDINE IS UNSUITABLE FOR CHRONIC CANCER PAIN

- Meperidine (e.g., Demerol) relieves pain for too short a period (about 2 hours, at most).
- Meperidine has poor oral availability (75 mg IV = 300 mg p.o.).
- Meperidine's toxic metabolite, normeperidine, causes seizures; it accumulates rapidly in patients with renal insufficiency.
- Meperidine is contraindicated in patients who are also taking monoamine oxidase inhibitors.

ety of acute pains, but it is not recommended for patients with cancer pain. It is inconvenient to give, and it can be dangerous.

Meperidine provides pain relief for only one to two hours. To provide around-the-clock relief, you would need to give the patient ten to twelve intravenous (IV) shots or six to twelve 50-mg pills at each dose (75 mg IV is equivalent to 300 mg p.o.; 150 mg IV equals 600 mg p.o.) (see Table 6.5). And meperidine is contraindicated for patients receiving monoamine oxidase inhibitors for depression or as part of a chemotherapy regimen. Meperidine has caused hyperpyrexia, seizures, and death in these patients.

Of equal concern are the potentially life-threatening side effects induced by meperidine's toxic active metabolite, normeperidine. At high serum levels, normeperidine causes seizures. In patients receiving frequent therapeutic doses of meperidine, high normeperidine levels can be reached rapidly. Normeperidine's half-life is 13 to 24 hours, and since it is renally excreted, its levels build even more quickly when the patient is dehydrated or has any impairment of renal function.

Normeperidine toxicity is easy to diagnose: 36 to 48 hours after beginning the meperidine (100 to 150 mg IV every 2 to 3 hours), the patient complains of not feeling well; he appears agitated and restless and may even manifest myoclonic jerking. If you do not stop the meperidine, the patient will develop seizures. And you cannot reverse the effects of normeperidine with naloxone—in fact, naloxone exacerbates these effects and is very likely to precipitate seizures in a normeperidine-toxic patient. Give the patient with toxic effects another opioid for pain relief and hope the normeperidine levels fall before a seizure occurs. If the patient does have seizures, use lorazepam to control these. To avoid painting myself into this corner, I do not prescribe meperidine for my cancer patients with chronic moderate to severe pain.

Temporal Aspects of the Pain. To decide which formulation of the opioid to prescribe, consider whether the pain is continuous, intermittent, or both. Most patients whose cancer is far advanced have both types of pain. To treat the continuous pain, I usually prescribe either a fentanyl transdermal patch or an oral sustained-release preparation of an opioid with a short half-life (i.e., morphine, oxycodone, hydromorphone, or oxymorphone) as the active agent.

Oral sustained-release preparations are formulated in a matrix that dissolves in the gut and releases opioid over 8 to 24 hours, depending on the preparation. As of 2014, only transdermal fentanyl and oral sustained-release morphine were available in generic formulations. Fentanyl patches are replaced every 48 to 72 hours; sustained-release morphine can be taken every 8 to 12 hours. OxyContin is the sustained-release form of oxycodone and is taken every 12 hours. Exalgo is a sustained-release form of hydromorphone that is taken daily. In 2005, the makers of Palladone, another form of sustained-release hydromorphone, withdrew it because of concerns of overdose if the pill was taken with alcohol. OpanaER is the sustained-release form of oxymorphone.

More rarely, as I discussed above, I use methadone, an opioid with a 24-hour half-life. Because of this long half-life, it is somewhat harder to titrate doses of methadone to the patient's pain level. I therefore generally choose methadone as the initial opioid only when there is a history of allergy to morphine, the patient's pain has a large neuropathic component, I need to give a long-acting preparation through a feeding tube (it comes in a liquid formulation), or I need to use the least expensive agent.

To treat intermittent pain or brief exacerbations of continuous pain, I prescribe a shorter-acting preparation of morphine, oxycodone, hydromorphone, or oxymorphone that can begin to provide relief in about 30 minutes to an hour. I might also prescribe as a rescue dose an immediate-acting preparation of oral transmucosal fentanyl citrate, which can begin to provide relief in as little as 10 minutes.

Routes of Administration

Once you have chosen an appropriate opioid, you need to decide the route by which it should be taken. Most patients will be able to use the oral route. Those with a feeding tube in place can receive medications through the tube. For cancer patients who cannot take oral medications, the transdermal, rectal, intravenous, or subcutaneous (SQ) route can be used. Step 2 agents (which include oxycodone in fixed combinations with NSAIDs, tramadol, and tapentadol) are available only in oral formulations. Table 6.4 indicates which formulations are available for each of the step 3 opioids listed (including pure oxycodone).

Opioids should not be given intramuscularly for either short- or long-term management of cancer pain. The injections are painful, and since absorption of the opioid is variable, they lead to unpredictable blood concentrations of the analgesic and provide suboptimal pain relief.

Oral route. Over 90 percent of patients can achieve effective therapy with oral or transdermal opioids. All the step 3 agents listed in Table 6.4 are available in oral formulations: various forms of transdermal fentanyl, as well as liquids, or immediate- or sustained-release tablets, pills, or capsules of other opioids. Patients with feeding tubes can safely use crushed tablets of methadone that dissolve completely in water, liquid methadone, or liquid immediate-release morphine, oxycodone or hydromorphone.

Oral Sustained-Release Agents for Patients with Feeding Tubes or Difficulty Swallowing Tablets. Most sustained-release preparations of morphine and oxycodone are designed to provide pain relief for 8 to 12 hours, but they may cause serious side effects if they are cut or crushed, because the full 12-hour opioid dose will be absorbed in an hour or two. There are morphine formulations (Kadian, Avinza) that consist of capsules containing polymer-coated sustained-release pellets from which the morphine is released. Because of this novel formulation, the capsules can be opened and the pellets sprinkled on food or put into a liquid such as orange juice or water, or they can be placed into a 16 French or larger gastrostomy tube in 20 ml of liquid. Do not attempt to put the beads through smaller gastrostomy tubes or a nasogastric (NG) tube. (Efficacy studies of absorption of the opioid from the pellets in patients with feeding tubes are currently in press.) Kadian is effective for 12 to 24 hours and is available in 20-, 50-, and 100-mg capsules. Avinza is effective for 24 hours and is available in 30-, 60-, 90-, and 120-mg capsules.

Oral Agents for Patients without Feeding Tubes but with Difficulty Swallowing Large Volumes of Liquids or at Risk of Aspiration. Concentrated (20 mg/ml) morphine (e.g., Roxanol) or oxycodone solutions (e.g., Intensol), given sublingually or bucally, are helpful for these patients. The efficacy of these agents is due in large part to their being swallowed and absorbed from the gastrointestinal tract in the same way that larger volumes are absorbed. Only about one-fifth of sublingual morphine solution or about one-third of sublingual methadone solution is absorbed, even when held under the tongue for 10 minutes (Weinberg et al. 1988). Sublingual buprenorphine tablets can provide relief for mild to moderate pain, but these are not available in the United States.

Transmucosal Agent. Several immediate-acting preparations of transmucosal fentanyl are now available in the United States. A patient must be taking the equivalent of 60 mg of oral morphine a day to be prescribed any of them as

rescue medication, and they can be given no more frequently than every 4 hours (www.TIRFREMSaccess.com).

The original version was available in the form of an oral sweetened lozenge containing 200 to 1600 mg of fentanyl citrate, attached to a handle. The fentanyl is easily absorbed transmucosally; it is effective in 75 percent of patients, produces rapid pain relief (in 10 to 15 minutes), and is well tolerated. There is no evidence of decreased effectiveness of this agent over time (median duration of use, 79 days; range, 1 to 423 days). The disadvantage of this formulation (brand name Actiq, but now also available in generic forms) is that the patient must "paint" the lozenge for about 3 to 5 minutes on the buccal mucosa. If the lozenge is sucked on, and the fentanyl swallowed, two-thirds of it will be wasted.

Other forms include a sublingual tablet (Abstral), a buccal tablet (Fentora), a buccal film (Onsolis) and nasal sprays (Lazenda, available in the United States, and Instanyl and PecFent [Lyseng-Williamson 2011], which in 2013 were not). The tablets and films are rapidly absorbed from normally moist mucosa, but the tablets dissolve poorly in patients who have undergone radiation to the head and neck, and are poorly tolerated in patients with mucositis. An excellent discussion of the comparable benefits of each of these forms was published in a comprehensive review of transmucosal fentanyl, published in 2012 (Twycross et al. 2012).

To prescribe any of the forms, clinicians must enroll in a risk-reduction, educational program, found at the website www.TIRFREMSaccess.com. When the medication is prescribed, the clinician must provide the patient with information on the product (also available at the website), and both the provider and the patient need to sign a consent form that must be faxed to the pharmacy. The lowest dose of the preparation must be prescribed first, but if that dose is not effective, the dose can be titrated. Since there is no relationship between the dose of the continuous baseline opioid the patient is taking and the dose of transmucosal fentanyl that will be effective (Knotkova et al. 2009), however, starting at the lowest dose is clinically reasonable. Although all transmucosal fentanyl preparations provide pain relief for only about an hour, they cannot be prescribed any more often than every 4 hours.

Topical route. Topical opioids may act through opioid receptors of all classes that are present in peripheral nerve terminals of inflamed tissue. These receptors appear in normal tissue within minutes to hours of the onset of inflammation (Stein 1995). Data demonstrating the efficacy of topical opioids are limited, but two randomized double-blind pilot studies support the use of topical morphine

in treating patients with decubitus ulcers (Flock 2003; Zeppetella et al. 2003). The gel has to be placed on open skin because it has poor bioavailability over intact skin (Paice et al. 2008).

Compounding pharmacies can add morphine to the IntraSite gel that is a standard treatment for stage II or III pressure ulcers. The gels are topically applied once to several times a day and covered with a standard dressing. The opioid-containing gels can provide equivalent or better relief of pain and cause fewer side effects than the higher doses of systemic opioids. Case reports suggest they are also useful for patients with open tumor infiltrates of the skin.

Transdermal route. The fentanyl patch is a transdermal fentanyl delivery system. It consists of a drug reservoir lined on the bottom by a rate-limiting membrane, which itself is attached to an adherent backing (Figure 6.2). The lipophilic opioid fentanyl is contained in the patch's drug reservoir; once the patch is attached to the skin, the fentanyl diffuses through the rate-limiting membrane into the fat in the skin. It is then absorbed into the bloodstream from this skin reservoir.

Buprenorphine is also available in a transdermal patch. In Europe, they are available in 35, 52.5, and 70 mcg/hr options and are changed every 72 to 96 hours. In one randomized placebo-controlled trial, cancer patients who were receiving 90 to 150 mg/day of oral morphine equivalents were switched to a buprenorphine

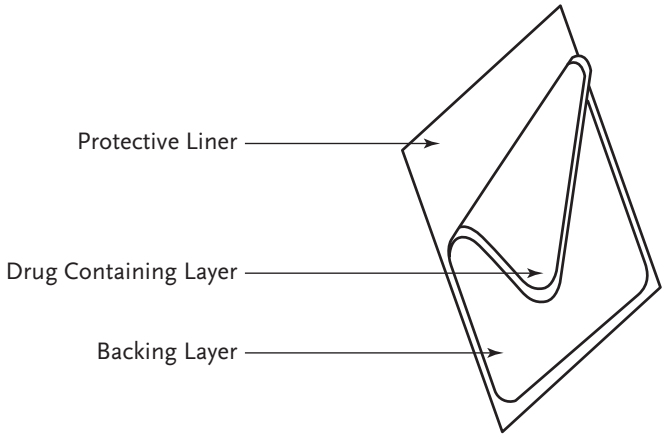

Figure 6.2. Duragesic patch. After the unit is placed on the chest wall, fentanyl, contained in the drug reservoir, diffuses through the release membrane into the skin. The drug is absorbed from the skin reservoir into the bloodstream. By 14 to 24 hours after the first patch is applied, blood levels of fentanyl are sufficient to provide pain relief. New patches are usually applied every 72 hours. From Janssen Pharmaceuticals, Inc.; with permission.

patch of 70 mcg/hr with satisfactory pain relief in 75 percent (Poulain et al. 2008). A consensus panel of European pain and palliative care experts concluded that transdermal buprenorphine was a valuable treatment for patients with chronic cancer pain (Pergolizzi et al. 2009). In the United States, we have access to only the lower-dose patches, of 5, 10, and 20 mcg/hr Butrans. Effective plasma levels are reached within 12 to 24 hours, and the patch is replaced every 7 days. These low-dose buprenorphine patches are likely to help only patients with mild to moderate pain.

Both fentanyl and buprenorphine can be used without dose reduction in patients with renal failure. Fentanyl is metabolized by the CYP3A4 cytochrome system in the liver, and its plasma levels can rise and patients can develop somnolence or respiratory depression if other drugs that are also metabolized by CYP3A4, such as ketoconazole, fluconazole, diltiazam, erythromycin, or verapamil, are added. For the same reason, pain may return if a patient has been stabilized on a fentanyl regimen while on one of these agents and that agent is discontinued. Unlike fentanyl, higher doses of buprenorphine (>20 mcg/hr) can prolong the QTc, and use of other QTc prolonging agents may be limited. I discuss these in the section on methadone, earlier in this chapter.

Because fentanyl is very rapidly metabolized by the liver, at least 12 hours are required to build up enough drug in the skin reservoir to establish an adequate blood level. By 14 to 20 hours, an effective, stable plasma concentration is reached and, in most patients, is maintained for a total of 72 hours. New patches are usually applied every 72 hours, though as many as 25 percent of patients find they need to replace the patches every 48 hours.

For many patients with stable chronic pain, transdermal fentanyl patches are useful as the sustained-release component of their pain regimen. The patches are especially helpful for those who are unable to take oral medications, who cannot tolerate other opioids, or who simply prefer a patch to taking pills even once or twice a day. In a randomized crossover study of patients who expressed a preference, significantly more preferred the fentanyl patches over oral sustained-release morphine (Payne et al. 1998).

The patch is not the best choice for managing the chronic pain of some types of patients. Transdermal fentanyl is not recommended for patients under 18 years old who weigh less than 110 pounds. And though I have not seen any studies documenting this observation, I and many of the nurses with whom I work have noticed that cachectic patients seem to get less relief using the patch. The patch must be placed on the skin over an area of fat into which the drug can diffuse. Do not place them over edematous areas, bony prominences, or tattooed skin. Since many hours are required to achieve a therapeutic drug level, the transdermal system is not indi-

cated for someone with acute severe or excruciating pain. In these patients, an opioid drip using morphine, fentanyl, or hydromorphone is more appropriate.

The patch can also be problematic for patients who have recurrent bouts of fever and infection, even simple urinary tract infections. During fevers, more drug is absorbed from the skin reservoir into the bloodstream, and the patient may develop a fentanyl overdose. In addition, if the patient becomes acidotic during sepsis, more drug will be liberated from albumin-binding sites. This "free" drug can also cause significant toxicity.

If the patient develops symptoms of overdose, removing the patch will not stop delivery of fentanyl into the bloodstream. Fentanyl continues to pass into the vasculature from the fatty skin reservoir until it is empty. Twenty-four hours after the patch is removed, the amount of fentanyl in the reservoir has decreased by only 50 percent. These patients may require a low-dose naloxone drip until the remaining drug is metabolized. To avoid precipitating a withdrawal syndrome due to the naloxone, use just enough to restore adequate respiration but allow the patient to remain asleep.

PRACTICE POINTS: CLINICAL IMPLICATIONS OF THE TRANSDERMAL FENTANYL DELIVERY SYSTEM

The fentanyl is deposited into a skin reservoir, from which it is absorbed. Therefore,

- Rescue dosing is needed for 12 to 24 hours while the reservoir is accumulating fentanyl.
- Used alone, the patch is not an effective initial treatment for patients with severe pain.
- For patients with severe pain, short-acting drugs should be used to establish the opioid dose that relieves the pain; then a fentanyl patch of appropriate strength can be placed.
- Toxicity can result from increased absorption during febrile episodes.
- In cases of overdose, 50 percent of the fentanyl is still present in the skin reservoir 24 hours after the patch has been removed.
- Patch placement is very important. Fentanyl must be placed over an area of fatty tissue; it cannot "travel" to the fat through edema fluid; tattoos also impair its absorption.
- The patch must adhere to the skin to deliver the fentanyl effectively; patches are not useful in patients with drenching sweats or in whom the patch cannot be placed flat onto the skin surface.

Despite these limitations, for many patients the transdermal system is a useful way to deliver a steady dose of a potent opioid. It is usually well tolerated and effective for patients who are medically stable and whose pain medication requirements do not vary markedly from day to day.

Rectal route. The rectal route of opioid delivery is especially helpful in a patient who is suddenly, unexpectedly unable to take oral pain medication. It is preferable to intramuscular injections and will provide effective relief. Tramadol, codeine, morphine, oxycodone, and methadone can all be given rectally. These drugs are available as commercially or custom-made suppositories, as custom-made gelatin capsules that enclose the oral long-acting formulation (e.g., MS Contin), or as elixirs that can be given as microenemas (i.e., in less than 30 ml of liquid) (Davis et al. 2002).

The sustained-release morphine preparations are as effective given rectally as orally, and the same or higher opioid blood levels are achieved after 24 hours (De Conno et al. 1995). Immediate-release oxycodone is absorbed generally in about 30 to 60 minutes and provides analgesia for 8 to 12 hours, though there is a great deal of variability from patient to patient (Leow et al. 1995). Hospice nurses suggest that before patients have the sustained-release tablet inserted, they have a soapsuds enema to remove any stool from the rectal vault. The tablet is then placed in the lower part of the rectum. Hospice pharmacies can often prepare customized suppositories containing the oxycodone, methadone, or morphine the patient was previously receiving.

The venous drainage from the rectum flows into a mix of portal and systemic circulation. Since morphine and oxycodone are extensively metabolized by the liver, avoiding the portal system maximizes the active blood levels you can achieve per dose but minimizes the levels of hepatically created active metabolites such as M-6-G. Unfortunately, colostomies are drained solely by the portal system; opioids placed in colostomies have less than half the bioavailability of those placed in the rectum.

Although placing sustained-release morphine or oxycodone tablets into the rectal vault is not approved by the U.S. Food and Drug Administration (FDA), morphine delivered by this route has been extensively studied and is safe and effective. Doses of rectal sustained-release morphine as high as 900 mg/day have been used.

Intravenous or subcutaneous routes. Patients with rapidly escalating pain, and those who are not getting relief from a transdermal patch, cannot swallow, do not have feeding tubes, or who have a bowel obstruction, need to have the opioid delivered by the intravenous or subcutaneous route. Opioids can be given

by either route continuously (to deal with the chronic portion of the patient's pain) and as bolus doses (to treat acute breakthrough pain).

The members of the Memorial Sloan-Kettering Cancer Center Supportive Care Program have developed guidelines to determine which patients will benefit from parenteral pain management at home.

Guidelines for Recommending Home Parenteral Opioid Therapy

- Parenteral pain management can be costly. We should discuss the cost/benefit of other routes and verify insurance coverage.
- The infusion can be deadly if not given correctly; we need to determine whether the infusion can be done safely: Who else is present in the home? Can they or the patient be taught how to manage the infusion? If the patient is alone, how will he or she be monitored?
- Do we feel we have adequate knowledge to manage the infusion, or is there a hospice physician available who has agreed to be responsible?
- Will the community hospice or home care system provide skilled personnel, including 24-hour nursing staff, on call for home visits?*

Intravenous Route. Intravenous morphine has the advantage of rapid action and easy dose adjustment. It is often offered as part of a program of patient-controlled analgesia (PCA).

PRACTICE POINTS: ADVANTAGES OF INTRAVENOUS OPIOIDS

- Prompt dose escalation in medically unstable patients with moderate pain who cannot use oral medication
- Rapid, precise, safe dose escalation for rapid relief of severe or excruciating pain
- Patient-controlled analgesia option

You are probably most familiar with PCA in the postoperative patient. These patients usually do not receive a continuous dose of morphine; they simply give themselves bolus doses as needed. A computer regulates the amount of drug given and how often a patient can dose himself; it records both how often the

*All guidelines modified from N. Coyle, N. Cherny, and R. Portenoy, Pharmacologic management of cancer pain, in *Cancer Pain Management*, 2nd ed., D. B. McGuire, C. H. Yarbro, B. R. Ferrell (eds), Boston: Jones and Bartlett, 1995.

patient asks for a dose and how much drug he actually receives. For example, the computer may record that the patient requested drugs twelve times in an hour but received it only four times, because the device was set to deliver a bolus dose only every 15 minutes. It also records the total 24-hour quantity of morphine delivered.

PCA is also for cancer patients. If I admit someone in pain, I often use an intravenous route with a basal opioid infusion and the PCA option or nurse-administered IV bolus doses because I can escalate doses quickly and precisely. If the patient has been taking opioids at home, I start the basal intravenous drip at an opioid dose equivalent to what I think she has been taking at home. Patients can also give themselves bolus doses, as needed, every 10 or 15 minutes, or a nurse can administer the boluses. The nurse carefully monitors the patient for pain relief and, if the patient is using a PCA, reviews the computer record for the total number of milligrams used. I use this information to increase the strength of the bolus whenever needed and, every 8 to 12 hours, to adjust the continuous-infusion dose (I explain this in detail later in the chapter). The opioid drip rate is increased until the patient's pain is relieved. If the patient was in pain because she was taking much less opioid than I prescribed, that quickly becomes apparent as well, and the drip rate can be lowered accordingly. When the required opioid dose has been determined, I transition the patient from the intravenous opioid to an oral sustained-release or a transdermal opioid at an equivalent dose along with a rescue oral opioid.

For patients with severe or excruciating pain, there is really no safer way to achieve adequate opioid plasma levels quickly than to do an intravenous opioid titration with IV bolus doses based on how much opioid the patient is already taking (Miaskowski et al. 2005). Later in this chapter you will find an example of how to do this titration. A patient might present with severe pain due to widespread bone metastases causing a combination of somatic and neuropathic pain. After careful titration, these patients are often found to need morphine infusions of 5 mg/hr or more (or 0.5 mg of hydromorphone) to relieve their pain. An infusion of 5 mg of morphine/hr would translate into 120 mg of sustained-release oral morphine every 8 hours (Table 6.5); that is, 5 mg/hr × 24 hr = 120 mg IV/day; 120 mg × 3 = 360 mg oral morphine/day. Even in an opioid-naïve patient, using the intravenous boluses, adding an intravenous infusion, and adjusting doses as needed, you will be able to reach 5 mg/hr in less than 12 hours. Using oral morphine alone, reaching a dose of 120 mg every 8 hours in an opioid-naive patient is likely to take much longer.

The intravenous route is also preferable for medically unstable patients who cannot use oral medications. For the reasons mentioned above, I would not pre-

scribe the transdermal fentanyl patch in these patients. If a patient with good pain control while taking oral medications needs to be NPO for surgery, I prescribe an opioid drip at a dose equivalent to his oral dose, then place him back on his oral medication as soon as possible.

Rare patients will not be able to tolerate oral medication and will either have contraindications to transdermal fentanyl patches or inadequate adipose tissue. Most of these patients will be able to use subcutaneous infusions if they desire, but some will prefer the intravenous route or require continuous intravenous infusions because of the volume of medication needed or the toxicity associated with delivering the medication subcutaneously.

If a patient has been receiving oral medications or using a transdermal patch, you simply need to convert the 24-hour oral dose to an intravenous one using the techniques detailed later in the chapter (see also Table 6.5). Many of these patients will already have an implanted vascular access device (e.g., a catheter or port) through which they can receive the infusions. If not, the patient will need a PICC line (peripherally inserted central venous catheter). Trained personnel can place PICC lines in patients in their home, and the catheters are easily maintained for the remaining two to three months of these patients' lives. Some home care agencies may require a chest x-ray to verify placement.

Subcutaneous Route. Some patients who cannot take oral medications and whose pain is unrelieved by transdermal fentanyl find subcutaneous opioid infusions effective. Ambulatory patients can use one of a variety of pumps that can provide both continuous infusion (for the chronic pain) and bolus medication (for breakthrough pains).

Morphine and hydromorphone (e.g., Dilaudid) are the most commonly used opioids in subcutaneous infusions. They are generally nonirritating and are well absorbed. You prescribe the same doses as for a continuous intravenous infusion. Methadone is less well tolerated subcutaneously and often induces a local reaction.

While most advanced-cancer patients need only the equivalent of 400 to 600 mg/day of morphine, about 10 percent will need more than 2000 mg. But even these very high doses can be delivered subcutaneously using an equivalent hydromorphone dose. One hydromorphone preparation (hydromorphone HP) delivers 10 mg/ml of hydromorphone, and 2 to 5 ml/hr is well tolerated subcutaneously. Using this preparation, you can easily deliver 30 mg/hr of hydromorphone with only 3 ml/hr of solution. This is the equivalent of 200 mg/hr of morphine, or 4800 mg/day of parenteral morphine. If necessary, the pharmacist can prepare even more highly concentrated solutions.

For the subcutaneous infusions, patients have a 27-gauge "butterfly" or Silastic needle inserted subcutaneously, usually on the anterior chest wall or in the abdomen. The site is changed every 5 to 7 days to minimize skin irritation. Many patients or their families are able to insert the needles themselves. Local inflammation is common but rarely is severe enough to warrant discontinuing the infusion. If it is bothersome, the patient can try changing to a different opioid to reduce the concentration or volume of the infusion or to eliminate allergic reactions to preservatives or impurities in the preparation.

Spinal opioids (epidural, subarachnoid). Spinal delivery of opioids produces pain relief because the exogenous opioids bind to receptors for the natural opiates (e.g., enkephalins) already present in the spinal cord. Nerves containing endogenous opiate receptors are present in the same area of the spinal cord that contains the synapses between afferent neurons and spinal interneurons. When either endogenous opiates or exogenous opioids bind to those receptors, they prevent the spinal interneuron from transmitting the pain signal up the spinal cord to the thalamus and cerebral cortex. Since the cortex does not receive the pain signal, the person does not experience pain.

Because epidural opioids are delivered locally into the epidural space and diffuse into the spinal fluid around the cord, they are effective at one-tenth of the doses required for the same opioid given peripherally. Subarachnoid opioids delivered directly into the spinal fluid are effective at one-hundredth of the systemic doses. Even though spinal opioids are absorbed into the systemic circulation, the side effects from these much lower doses are usually milder.

Spinal opioids can be used alone or with anesthetics, alpha-adrenergic agents, or baclofen (for spasticity) to improve their efficacy or to minimize the opioid-induced side effects. They can be delivered via either temporary epidural catheters or permanent epidural or subarachnoid catheters. Patient-controlled epidural analgesia (PCEA) or intrathecal analgesia, by which patients self-administer a bolus of spinal opioid, are also available.

Implantable Intrathecal Drug Delivery Systems. A randomized trial comparing implantable intrathecal drug delivery systems (IDDS) with conventional medical management delivered by an expert pain team demonstrated some surprising findings (Smith et al. 2002, 2003). This trial enrolled 202 patients who were taking at least the equivalent of 200 mg of oral morphine a day and were unable to achieve satisfactory pain relief with standard therapy, even when managed by pain experts, or who were taking less than 200 mg oral morphine equivalent per day but were suffering intolerable side effects from what otherwise was satisfactory relief of their pain. If the conventional management was ineffective, an IDDS was offered. Significantly more of the patients given an IDDS

had a greater than 20 percent reduction in their pain and in side effects related to the treatment (38 percent vs. 58 percent), particularly fatigue and sedation. These differences likely resulted from the lower systemic opioid doses required to control the pain. More unexpected, however, was that patients with IDDS lived longer! The patients were more alert, less fatigued, and in less pain, and perhaps they had increased mobility; all these may have contributed to the documented increase.

Anesthesiologists who specialize in pain management typically place and manage both temporary and permanent epidural and intrathecal infusions. I offer below a general overview of the use of these routes. More detailed discussions of the devices used, the insertion techniques, and the management of the catheters are provided in the bibliography at the end of the chapter.

PRACTICE POINTS: ADVANTAGES OF SPINAL OPIOIDS

- Spinal opioids can treat refractory neuropathic pain resulting from injury to peripheral nerves.
- Opioids, anesthetics, alpha-adrenergic agents (e.g., clonidine), and other drugs are infused.
- Temporary infusions can be used to
  - —Help patients regain sensitivity to lower systemic opioid doses.
  - —Determine whether the epidural route provides effective pain relief. If so, a permanent catheter may be placed.
- Patient-controlled epidural and intrathecal analgesia is available.

Indications. Spinal opioids benefit those patients whose neuropathic pain syndrome is not responding to systemic opioids, or who require such high systemic opioid doses that, despite the use of appropriate adjunctive agents, the side effects are intolerable.

Temporary infusions or boluses of epidural opioids are most commonly used to manage postoperative or obstetric pain. Temporary catheters are placed before surgery, and opioid solutions are given as a bolus or infused (e.g., Duramorph). The infusions or boluses are repeated as needed in the next several days, and the catheter is then removed.

Temporary opioid/anesthetic or opioid / alpha-adrenergic agent (such as clonidine [e.g., Duraclon]) infusions are used in a rare cancer patient to enable him to regain sensitivity to lower doses of systemic opioids. Even in these patients, systemic opioids usually are not stopped entirely, because many patients have pain in areas outside the areas treated by the spinal infusion. For example

a patient might have chest wall pain from bone metastases eroding through the skin along with severe lower extremity pain from nerve plexus involvement. The spinal catheter alleviates the lower extremity pain, but systemic opioids are needed for the chest wall pain. The systemic opioid dose is usually much lower after an epidural or intrathecal infusion is begun. Close collaboration with your anesthesia pain consultant will ensure that this is done safely without pain exacerbations or opioid-induced toxicity. The spinal opioid infusion is considered a success if the dose of systemic opioid can be lowered enough that the associated side effects become tolerable.

Other patients, such as (but not limited to) those with bilateral severe neuropathic pelvic pain due to recurrent colorectal, bladder, or gynecologic cancers, receive temporary catheters to determine whether opioids and anesthetics given via the epidural route will provide satisfactory pain relief. If the temporary infusion reduces the patient's pain by at least 50 percent, she is considered to be a good candidate for insertion of a permanent epidural Port-a-Cath. The device is identical to the one used for intravenous infusions. The port is implanted subcutaneously in the skin of the abdominal wall, and the catheter is in the epidural space, instead of in the vascular space.

NEURAXIAL DRUG DELIVERY SYSTEMS

- Temporary (1 to 4 weeks): Percutaneous epidural or intrathecal catheter.
  —Taped to patient's back (for diagnostic infusions).
  —Tunneled 1 to 2 inches from insertion site (for therapy).
- Intermediate (1 to 2 months)
  —Tunneled epidural catheter attached to implanted injection port.
- Permanent (years): Implanted intrathecal catheter.
  —Attached to totally implanted programmable pump for intrathecal infusions.

The infusion systems vary from cassettes connected to the subcutaneously inserted port of an epidural infusion to the totally implantable intrathecal delivery systems with programmable infusion pumps. Because of the cost associated with the implantable infusion systems, it is recommended that they be inserted only in patients who are expected to live at least three months.

Epidural versus Intrathecal Catheter Placement. Anesthesia pain specialists can place permanent catheters in either the epidural or the intrathecal spaces. The choice of the totally implantable intrathecal pump over the epidural for a permanent catheter depends on the experience of the clinician, the needs and

life expectancy of the patient, and the expertise of the home care teams. Extensive preoperative education of the patient and the family is required before any permanent catheter is inserted.

Intrathecal catheters connected to totally implanted pumps have several advantages over epidural catheters. Intrathecal opioids act more quickly and for a longer time. In addition, only 10 percent as much opioid is needed because it is delivered into the spinal fluid, not the epidural space. Because of the lower opioid doses required, patients experience fewer systemic opioid-induced side effects. The implanted pumps require no maintenance, and their reservoirs require infrequent (usually monthly) drug refills.

PRACTICE POINTS: COMPARISONS OF INTRATHECAL (IT) AND EPIDURAL CATHETERS

Advantages of IT Catheters

- Smaller drug volume
- Fewer systemic side effects
- Lower incidence of fibrosis if used for 3 to 6 months
- Pump refills needed only monthly vs. weekly epidural cassette replacement
- No risk of needle from cassette to port being dislodged
- No home care services required

Disadvantages of IT Catheters

- Increased incidence of meningitis
- Cost of totally implanted system

Totally implanted pumps connected to intrathecal catheters are also considered when a patient is expected to live more than three months, because, over time, epidural catheters are more frequently obstructed by fibrosis. They are also indicated for patients who cannot tolerate the volume of epidural infusion that they would need for pain relief.

While the intrathecal site can be beneficial, it also has disadvantages. Though intrathecal catheters allow access to the spinal fluid for sampling, infections of intrathecal catheters can more easily induce meningitis. And their insertion requires a totally implantable delivery system with a subcutaneous infusion pump, which alone can cost more than $50,000.

Drugs Used in Spinal Infusions. Morphine or hydromorphone are the opioids most commonly used in epidural and intrathecal infusions. They are

hydrophilic drugs, not very lipid soluble, and take quite a while to diffuse across the meninges and into the cord. But they also remain in the cerebrospinal fluid (CSF) and are bound to the spinal cord opioid receptors for a long time. Because they migrate to other spinal segments, the spinal catheter does not have to be placed directly over the affected segment for the infusion to be effective.

More lipid-soluble opioids such as fentanyl or sufentanil are also used in spinal infusions. They are potent spinal analgesics, but because they don't migrate in the CSF, their effectiveness depends on precise catheter placement.

The dose of the epidural opioid is based on the daily amount of intravenous opioid the patient has been receiving. Epidural infusions start at one-tenth of the total daily parenteral opioid dose, given over 24 hours; for intrathecal infusions, only one-tenth of the *epidural* dose is required. For a patient on a 10 mg/hr morphine drip, the calculation would be as follows:

10 mg/hr parenteral morphine = 240 mg / 24 hr parenteral morphine
(240 mg / 24 hr) / 10 = 24 mg over 24 hours for the epidural dose
(24 mg / 24 hr) / 10 = 2.4 mg over 24 hours for the intrathecal dose

The spinal morphine is given as a continuous infusion (i.e., 1 mg/hr epidural or 0.1 mg/hr intrathecal infusion).

Local anesthetics (e.g., bupivacaine), alpha-adrenergic agonists (e.g., clonidine), and baclofen (e.g., Lioresal) are also given by spinal infusion. Infused alone or added to opioid solutions, bupivacaine and clonidine can provide pain relief for patients who do not get relief from opioids alone, and they can minimize the side effects of the opioids by decreasing the doses needed for pain relief. Bupivacaine is the most commonly used anesthetic agent; the starting dose of intrathecal bupivacaine is 3 mg/day, and it is escalated as needed. Rarely, epidural infusions of 0.125 to 0.150 percent bupivacaine cause sensory or motor impairment. Baclofen is effective in relieving neuropathic pain and spasticity, with few associated side effects compared with oral administration. Doses used are 100 to 1000 times less than oral doses. More rarely, somatostatin, octreotide, calcitonin, ketamine, or midazolam are infused.

Side Effects of Spinal Opioids and Anesthetics. Opioid-naive patients who receive epidural opioids for pain relief after surgery experience pruritus, nausea, vomiting, urinary retention, constipation, and more rarely, respiratory depression. The vast majority of cancer patients requiring spinal opioids, however, are not opioid-naïve, and they rarely develop these side effects. If they do, small doses of naloxone (a 40-μg bolus followed by a continuous infusion starting at 5 μg/kg/hr) can reverse the side effects without eliminating analgesia. Compared with the opioid-naive patient with nonmalignant pain, cancer patients

may require much higher spinal opioid doses. As these doses are absorbed into the circulation, the patient may become sedated. Very high intrathecal opioid doses can cause the patient to develop myoclonic jerking.

PRACTICE POINTS: SIDE EFFECTS AND DRUG- AND CATHETER-RELATED COMPLICATIONS OF NEURAXIAL INFUSIONS

- Pruritus, nausea, vomiting, and urinary retention are rare in patients taking systemic opioids.
- Depending on the dose infused, patients may have typical opioid-related side effects.
- Anesthetic may induce hypotension.
- Placement-related complications include superficial bleeding (or, very rarely, hematomas compromising the cord or the cauda equina), abdominal or retroperitoneal organ or lung perforation, nerve root damage, seromas, postspinal headache in up to 20 percent of patients receiving subarachnoid catheters.
- Catheters become dislodged, tear, kink, or become plugged by fibrosis or catheter-related granulomas.
- Patients may underdose or overdose as a result of errors in refilling or programming.
- CNS or skin infection may occur.

The side effects caused by anesthetics used intraspinally are due to the sympathetic blockade they induce as well as their systemic absorption. Depending on the location of the catheter, patients may become hypotensive initially, so they are usually given concomitant intravenous fluids when the infusion is begun. In animal studies, bupivacaine caused both systemic and local toxicities, including seizures, cauda equina syndrome, and impaired sensation. In clinical trials, although patients might experience dose-dependent local toxicities, systemic effects were rarely seen, possibly because the bupivacaine is so highly protein bound. The neurologic side effects are not reported for bupivacaine doses of less than 25 mg / 24 hr (Du Pen et al. 1992).

Catheter-Induced Complications. The most common complications of spinal infusions arise during catheter implantation or from the catheters themselves. Permanent catheters are inserted following administration of local anesthesia and tunneled subcutaneously to an implanted injection port. During implantation, bleeding can occur superficially or, very rarely, in the epidural space, where it can cause an epidural hematoma, spinal cord compression, or a cauda

equina syndrome that may require emergency neurosurgery. Other surgery-associated problems include perforation of an abdominal or retroperitoneal viscus or lung by the tunneling needle, or damage to nerve roots or the cord by the needle or the catheter itself. Patients also may develop pump pocket seromas, which usually require no specific therapy.

Catheters can dislodge, kink, or tear. Epidural catheters can also cause epidural fibrosis when in place for several months, which occasionally leads to cord compression. The fibrosis can also restrict the migration of the drug and decrease its efficacy. Catheters may even have to be repositioned.

Fibrosis is not a problem with catheters in the intrathecal space, but there can be catheter-associated granulomas. Postspinal headache due to CSF leaks occurs in up to 20 percent of patients with intrathecal catheters. If the headaches persist, epidural blood patching is necessary.

Other Complications. Errors in refilling or programming the continuous-infusion pumps can lead to serious or even life-threatening complications. Anesthesia pain specialists minimize this risk by ensuring that only properly trained individuals perform these tasks and that they check their work meticulously. If an error is discovered that might cause an overdose, the patient is immediately hospitalized for observation and treated symptomatically (e.g., naloxone for respiratory depression, anticonvulsants for seizures). Underdosing due to kinks or other problems with the catheter or the infusion pumps or mixtures can result in recurrence of severe pain.

With very long-term use, patients can develop impotence (reversible with testosterone), amenorrhea, and other endocrine abnormalities. Edema of the hands and feet also occurs and is only partially responsive to elevation and diuretics.

Infection is the most serious complication. Implanted epidural catheters have an infection incidence of 8 percent, but the infection is usually limited to the skin around the injection port and the subcutaneous track of the catheter. If the injection port and catheter are removed promptly, the infection rarely progresses to an epidural abscess.

Contraindications. Certain medical and social situations preclude the use of spinal opioids. Patients with bleeding diatheses or active septicemia cannot have the catheters placed. Diabetics and immunocompromised patients have higher rates of septicemia, but these are not absolute contraindications. Epidural metastases can lead to CSF obstruction, but catheters can be placed rostral to the obstructing lesions.

As with continuous-infusion opioid therapy, cost and maintenance issues must be addressed. Will the patient or family be able to care for the catheter? Does their insurance cover the devices and the home care services required or

can a source of financing be identified? Are physicians and home care services available to manage the infusions and the catheters or reprogram or refill the implanted pumps at home?

Caring for Patients Receiving Spinal Opioids. Anesthesia pain specialists along with their specially trained nurses and home care service nurses care for patients with spinal catheters as both inpatients and outpatients. They work with the patients' families and with the home care and hospice services that are helping patients and their families maintain the catheters at home.

Summary. Spinal infusions add significantly to the quality of life of those rare patients who need them. I have seen patients with severe thoracic or bilateral lower abdominal or pelvic pain, unable to tolerate systemic therapy or continuing to feel intolerable pain, experience a marked improvement in their day-to-day existence while receiving an infusion of a spinal opioid / anesthetic, with or without clonidine. I urge you not to hesitate in referring patients who might benefit from this treatment to anesthesia pain specialists.

Preventing and Relieving Side Effects of Opioids

For many patients, especially older ones, it is not enough that opioids relieve their pain. More than 75 percent of patients are concerned that if they take opioids, they will develop constipation, nausea, drowsiness, confusion, or manifestations of delirium such as nightmares and hallucinations. Even side effects that seem minor to us can persuade patients that these drugs are not for them, so side effects must be prevented whenever possible and treated aggressively if they occur.

Constipation

Constipation is the most common side effect of opioid therapy, occurring in almost everyone who takes opioids, even in those with colostomies. In my experience, the only exceptions are patients with total gastrectomies or those with gastric or jejunal feeding tubes, whose diet consists mainly or entirely of liquid enteral nutrition.

Searching for a Natural Solution

Mr. Samuels, a former longshoreman, was such a patient. He was suffering from recurrent colon cancer that invaded his sacrum. As you can imagine, his pain was excruciating, and we hospitalized him to bring it under control as quickly as possible. After a few days of escalating doses of intravenous morphine, he told us that his pain control was satisfactory. We switched him to the equivalent dose of an

oral sustained-release preparation, which, in his case, was 60 mg of morphine every 8 hours, and discharged him.

When we saw him a week later, his pain was again excruciating. He told us that he didn't like the "artificial laxative" we had prescribed (lactulose syrup), and therefore he did not take any of it. When he became constipated, he quite accurately attributed his constipation to the opioids, and he stopped taking them as well. He said he preferred the pain to being constipated—that a daily bowel movement was very important to him. It was only when we discussed the fact that a more "natural" laxative was available, and he purchased some senna from a health food store, that he agreed to resume his opioids.

Even patients taking step 2 opioids develop constipation. In one hospice study (Bruera et al. 1994), for example, 40 percent of those not receiving opioids, 63 percent of those on step 2 opioids, and 87 percent of those taking step 3 opioids required laxative therapy. Unfortunately, constipation is one side effect that usually does not diminish with time. The gut does not accommodate or return to its normal pattern. I strongly recommend, therefore, that you prescribe routine, not as needed, stool softeners and laxatives for any patient beginning opioid therapy.

A number of factors may contribute to constipation in cancer patients with pain. Inactivity, lack of a private place to defecate, poor food or fluid intake, hypercalcemia and hypokalemia, peritoneal studding with cancer, bowel obstruction, as well as damage to the spinal cord, cauda equina, or peroneal nerve plexus can induce constipation even in patients not receiving opioid pain medications. So can a number of drugs, including anticholinergics, calcium-containing antacids, calcium channel blockers, diuretics, opioid adjuvant agents such as tricyclic antidepressants and phenothiazines, octreotide, and serotonin antagonists used as antiemetics (e.g., ondansetron).

The type of opioid may also be a factor, though this is controversial. In two systemic reviews, however, transdermal fentanyl was less constipating than oral sustained-release morphine (Tassinari et al. 2008 and 2009). In Europe, patients can use the combination agent Targin to minimize opioid-induced constipation if they require no more than 80 mg of oxycodone a day. Targin is a preparation that combines sustained-release oxycodone with sustained-release naloxone; the naloxone acts directly on the gut mucosa to decrease opioid-induced constipation and does not decrease pain relief (Simpson et al. 2008). Unfortunately, the lifestyle changes and medications we normally recommend to patients with constipation who are not taking opioids are not likely to be effective for patients who need opioids. Increased water intake, increased activity, fiber therapies, or disodium disuccinyl docusate (e.g., Colace) are generally fine for people who are con-

stipated, but won't work for patients on opioids; insoluble fiber is likely to exacerbate the problem. Even if the patient is able to take the amount of water needed and get some exercise, the slowed intestinal transit time makes insoluble fiber therapy ineffective in this population. And patients often feel bloated or "full," further impairing what may be an already diminished appetite.

Mechanism. The difference lies in the effect of the opioids on intestinal motility (Walters and Montagnini 2010). The bowel normally empties through coordinated waves of peristaltic movements that are more frequent in the first half of the day. Inactivity itself reduces these waves and increases the colonic transit time from the normal 2 to 3 days to between 4 and 12 days.

In contrast, the bowel of a patient on opioids is in a state of muscle "fibrillation"; the intestinal muscles are unable to produce the normal coordinated peristalsis, colonic mucosal secretions are decreased, and colonic transit time and the time for water to be reabsorbed from the stool are prolonged. Although the gut has opiate receptors, it is unlikely that these effects are due entirely to the local receptors. Patients taking parenteral opioids also suffer from constipation, and switching from oral to parenteral opioids does not completely reverse the problem. In addition, opioids increase the tone and decrease the sensitivity of the anorectal sphincter, which then does not relax appropriately. This side effect further predisposes older patients, who already have decreased sphincter sensitivity, to opioid-induced constipation.

PRACTICE POINTS: TREATING OPIOID-RELATED CONSTIPATION

- All patients taking step 2 or 3 opioids need routine (not p.r.n.) prophylactic laxatives.
- Discontinue insoluble fiber (e.g., Metamucil).
- Give osmotic agents (e.g., polyethylene glycol) or agents that stimulate the myenteric plexus (e.g., senna). Reserve lactulose for lactose-tolerant patients.
- Increase the laxative dose as the opioid dose increases.
- Consider using a combination product of sustained-release opioid and sustained-release naloxone (e.g., Targin) where available.
- In patients taking opioids without laxatives, diarrhea or urinary incontinence suggests impaction.
- Opioid bowel syndrome may respond to motility agents (e.g., metoclopramide) or to opioid antagonists (naloxone or methylnaltrexone).
- If the syndrome does not respond to motility agents, methylphenidate and clonidine can prevent withdrawal while the opioid dose is lowered.

Therapy. A number of bowel regimens have been published, but none has been studied in a controlled fashion. (Sources for a number of these are provided at the end of the chapter.) Table 6.6 indicates the drugs most commonly used to prevent or treat constipation, along with their mechanism of action, recommended doses, and frequency of administration.

Agents that stimulate the myenteric nerve plexus, such as senna (e.g., Senokot) and bisacodyl (e.g., Dulcolax), and osmotic agents, such as magnesium hydroxide (e.g., Milk of Magnesia), magnesium citrate, lactulose/sorbitol, and polyethylene glycol (e.g., Miralax), are the most effective agents. Senna is usually given at a starting dose of two tablets twice a day and can be increased to three to four tablets two or three times a day as needed. Bisacodyl is started at two tablets at bedtime, to be repeated in the morning if necessary. It can be increased to two to three tablets two or three times a day if needed.

Lactulose is given at much lower doses than are needed for patients with hepatic encephalopathy. It is effective at 15 to 30 ml at bedtime but can be increased to 60 ml every 6 hours as needed. Lactulose, however, can cause excessive gas and cramping in the many patients we see who are lactose deficient (Teuri et al. 1999). Other patients become lactose deficient during therapy, when chemotherapy agents denude their gastrointestinal mucosa. Should those patients become constipated because of opioids, I would use polyethylene glycol (e.g., Miralax), instead of lactulose, starting at 17 g in 4 to 8 oz of liquid once a day. All the stimulants are of course contraindicated in patients with bowel obstruction.

Patients on opioids who have extensive peritoneal carcinomatosis, who have longstanding diabetes mellitus, or who have had problematic constipation in the past may remain constipated despite all these measures. Methylnaltrexone is designed for these patients. Methylnaltrexone is a peripheral opioid receptor antagonist that, unlike naloxone, does not cross the blood-brain barrier. It reverses opioid-induced constipation in about 50 percent of patients, works within one to two hours, and causes no increased pain or evidence of opioid withdrawal (Table 6.6) (Portenoy et al. 2008; McNicol et al. 2008; Chamberlain et al. 2009; Becker and Blum 2009).

I have found a combination of senna and an osmotic agent (sorbitol or polyethylene glycol) to be effective and well tolerated by patients on opioids. When you first prescribe tramadol or even a low dose of opioid, also prescribe a bedtime laxative, such as one or two senna tablets per day. Explain to patients that to maintain regular bowel movements, they must take the laxatives daily, even if they have had a bowel movement that day.

Patients taking step 3 opioids such as sustained-release morphine or oxycodone or transdermal fentanyl may need as many as twelve senna tablets in divided doses, along with a bedtime osmotic agent as needed (e.g., 17 g of polyethylene

glycol). As mentioned above, polyethylene glycol is likely to have fewer side effects than lactulose, and it is more effective for patients with chronic constipation (Lee-Robichaud et al. 2010). Generally, the more opioid, the more laxative a patient needs. The goal is for patients to have one soft bowel movement every one or two days.

PRACTICE POINTS: LAXATIVE ESCALATION

- Initial regimen:
  - —Senna (e.g., Senokot + Colace or Senokot-S) ± polyethylene glycol p.r.n. h.s. if no stool in 48h
    or
  - —Bisacodyl h.s. ± polyethylene glycol
- If ineffective:
  - —Escalate doses of initial agents (e.g., three senna tablets b.i.d. or t.i.d. plus 17 to 34 g of polyethylene glycol, or 30 to 60 ml of lactulose in lactose-tolerant patients).
- If patient is obstipated:
  - —Add Milk of Magnesia + mineral oil or magnesium citrate
    or
  - —Increase lactulose up to 60 ml q.i.d. or increase dose of polyethylene glycol.
- Use methylnaltrexone SQ every other day for patients whose opioid-induced constipation remains refractory.
- If patient is impacted, prior to using methylnaltrexone:
  - —Lubricate rectum, disimpact, and give enemas until clear.
  - —Institute appropriately aggressive prophylactic regimen.

If a patient becomes obstipated, you may need to add magnesium hydroxide (e.g., Milk of Magnesia) (30 to 60 ml) plus mineral oil (15 to 30 ml) daily or twice a day, magnesium citrate (8 oz), or enemas, as well as adding a dose of lactulose (30 to 60 ml), but these agents are less well tolerated and are not usually needed as part of a routine regimen. You can also increase the polyethylene glycol to two to four times a day. For paraplegic patients, a cup of polyethylene glycol two to three times a day is usually effective.

If your patient is hospitalized, you need to ensure that the house staff does not write the laxative order as "p.r.n." Patients in pain do not think to ask for a laxative. They only realize that there's a problem when, a week or so later, they have not had a bowel movement.

Impaction. Fecal impactions can occur when patients are not prescribed a laxative or do not take one. Older patients, especially those who are confused, are particularly susceptible to this problem because their decreased rectal sensitivity allows a large mass of stool to form. These impactions may be difficult to diagnose, as patients and their families may not be aware of them. Rather than complain of constipation, the patient may instead complain of symptoms caused by the pressure of the fecal mass, or urinary incontinence or diarrhea, which is actually stool passing around the impaction through a sphincter that has become incompetent.

Since 90 percent of impactions occur in the rectum, they are easily diagnosed by digital rectal examination. They are readily treated by lubricating the rectum and doing a manual disimpaction, followed by saline rectal lavage or enemas. Glycerine suppositories or mineral oil enemas may be required to soften the impaction. After the impaction is cleared, you can institute one of the prophylactic regimens outlined above.

Opioid bowel syndrome. A very small minority of patients develop the so-called opioid bowel syndrome. Unlike impaction, this syndrome is caused by a functional, not a mechanical, bowel obstruction. Patients with this syndrome experience nausea, vomiting, abdominal distention, and mild abdominal pain. The pain will exacerbate if higher opioid doses are used to treat it.

If there is no mechanical bowel obstruction, you will often be able to reverse the syndrome with an agent that increases bowel motility, such as metoclopramide (e.g., Reglan) orally or intravenously, or methylnaltrexone, discussed above. There is no longer any need to use naloxone orally.

On occasion I have found that the syndrome would not reverse until I lowered the dose or even totally discontinued the opioid. If you must lower the opioid to less than 25 percent of the previous dose, you will need to prevent opioid withdrawal. Withdrawal symptoms after chronic opioid use are mediated in part by increased activity of noradrenergic neurons, which can be blocked by clonidine or lofexidine. Clonidine has been successfully used at 0.1 to 0.2 mg (p.o.) every 4 hours for heroin users, tapered after day three for a total of ten days. Cancer patients may be treated with a clonidine patch, 0.1 to 0.2 mg / 24 hr. If insomnia or muscle cramps appear, chlordiazepoxide is recommended. Lofexidine, 0.2 mg titrated up to 1.2 mg twice daily, can also be used (Kosten and O'Connor 2003). A palliative care consultant or hospice medical director can help you control the patient's pain at the lower doses of opioids.

Nausea

Nausea is also a very common side effect of certain opioid agents. If no antiemetics are given, one-half to two-thirds of patients who take oral codeine or

morphine for the first time will develop nausea or vomiting. These patients may mistakenly think that they are allergic to the opioid. If you don't warn them about this side effect, you may not be able to convince them to continue taking these agents, even if they have been effective in relieving the pain.

To prevent nausea in opioid-naive patients, consider adding prophylactic prochlorperazine (e.g., Compazine) (10 mg p.o. t.i.d. or q.i.d.) or warning patients and their families that nausea may develop, that it is likely to last only a few days, and that you can relieve it with prochlorperazine. Some patients require as much as a week of therapy, but most patients do not experience nausea for more than seven days despite continued opioid therapy.

PRACTICE POINTS: TREATING NAUSEA IN PATIENTS TAKING OPIOIDS

- Eliminate other contributing factors (constipation, gastritis, peptic ulcer disease, gastric outlet or bowel obstruction, hypercalcemia, hyponatremia, hepatic or renal failure, CNS disease).
- Warn opioid-naive patients about transient nausea or prescribe a prophylactic antiemetic.
- Consider lowering the opioid dose for patients who develop nausea after receiving other treatments to eliminate the painful condition (e.g., radiation therapy).
- Give a different opioid agent.
- Add neuroleptics (e.g., prochlorperazine) for patients with nausea and vomiting.
- If prochlorperazine is not effective, discontinue and replace with ondansetron.
- Consider a gastric motility agent (e.g., metoclopramide) for patients with nausea, vomiting, early satiety, or bloating after eating.
- Give antivertigo agents (e.g., meclizine) if nausea is induced by movement.

If patients taking opioids develop nausea later in the course of their treatment, other etiologies must be eliminated. Other common causes of nausea in cancer patients include chemotherapy, radiation therapy, constipation, gastritis or gastric ulcer disease, gastric outlet or bowel obstruction, hypercalcemia, hyponatremia, hepatic or renal failure, or disease of the CNS. If the nausea is due to one of these problems, it will usually be relieved if you can eliminate the

cause. Constipation, for example, is a common, easily reversible cause of nausea in these patients.

If none of these problems is present, late-developing nausea in a patient taking opioids may be an indication that the patient's pain is diminishing, and his opioid dose should be lowered. Consider, for example, a patient who is receiving radiation therapy for a painful bony metastasis and has been taking an opioid to relieve the pain until an adequate radiation dose could be given. Weeks later, although the pain from the metastasis has diminished significantly, the patient is still taking the same opioid dose and, as a result, develops nausea. In such a case, simply lower the dose of the opioid agent. The nausea usually disappears promptly, and the pain relief remains satisfactory.

Other patients being treated with opioids will develop nausea as they begin to take a higher dose of opioid to treat an increased intensity of pain. In these cases, if you substitute a different opioid agent, the nausea often disappears. If the patient has been receiving morphine, for example, substitute an equianalgesic dose of hydromorphone (e.g., Dilaudid) or fentanyl.

Therapy. If none of the maneuvers described above is effective, try to determine the mechanism by which the opioid is producing nausea and use the agent(s) most efficacious in reversing the problem (see Table 6.7). Treatment of chemotherapy- and radiotherapy-induced nausea is reviewed in Chapter 9.

Patients who have nausea without vomiting are likely suffering because opioids stimulate the chemoreceptor trigger zone in the medulla (the area in the brain that is responsible for chemotherapy-induced nausea), which activates the vomiting center there. These patients may benefit from neuroleptics such as haloperidol (1 to 2 mg p.o. every 8 to 12 hours or 0.5 to 1 mg parenterally every 8 to 12 hours), prochlorperazine (10 mg p.o. t.i.d. to q.i.d. or 25 mg p.r. every 12 hours), or olanzapine (Zyprexa, Zydis) (2.5 to 5 mg p.o. h.s. or b.i.d.), which block the transmission of the signal to the medulla's vomiting center.

Delayed gastric emptying is another likely cause. Metoclopramide, with its dual sites of activity (blocking the chemoreceptor trigger zone and enhancing gastric emptying), is the agent of choice for these patients. Metoclopramide is very effective even in low doses (5 to 10 mg b.i.d. to q.i.d. or 1 to 3 mg/hr IV). It can also be given rectally at the oral dose, either by suppository (if available) or through rectal administration of the tablets or liquid drug.

The 5HT3 receptor inhibitors like ondansetron (e.g. Zofran) are effective in chemotherapy- or radiotherapy-induced nausea and may be efficacious in any type of opioid-induced nausea (4 to 8 mg p.o. or IV b.i.d. or t.i.d.). Corticosteroids, also effective in chemotherapy-induced emesis, and mirtazapine, which has antiemetic properties, have not been studied in the treatment of opioid-

induced nausea but an empirical trial is warranted in patients who are refractory to the other therapies.

Patients taking opioids who complain of nausea along with movement-induced vertigo usually benefit from agents such as scopolamine (transdermal patch or 0.3 mg t.i.d. p.o. or SQ) or meclizine (Bonine, Antivert) (25 mg t.i.d. p.o.).

Sedation

Sedation can be an important dose-limiting side effect in patients taking opioids. It can lead patients to limit the opioids they will take, even though their pain remains uncontrolled. Like nausea, sedation is most prominent when the patient first begins taking opioids and lessens within a few days, even if the dose remains the same. Studies have shown that, after the first two weeks of patients taking sustained-release opioids, no psychomotor impairment remains, and it is safe for patients to drive again as long as they do not take immediate-release opioids sooner than 2 hours before or during the time they are driving (Fishbain et al. 2003; Vainio et al. 1995). A comprehensive, structured, evidence-based review indicates that for patients taking long-term opioids, there is moderate to strong consistent evidence for lack of impairment of psychomotor abilities, even immediately after taking a usual dose of opioids (Fishbain et al. 2003). The review also found no higher incidence of accidents or motor vehicle violations, and no impairment as tested in on- or off-road driving simulations. Evidence on cognitive impairment, however, was inconclusive.

PRACTICE POINTS: MINIMIZING SEDATION

- If state laws permit driving while taking opioids, advise patients to avoid driving for at least 2 weeks after sustained-release opioids or methadone are initiated or dose is increased, and not to take *any* immediate or short-acting opioids within 6 hours before or while driving.
- Don't mistake "catch-up" sleep for oversedation.
- Give sustained-release agents for baseline pain control, immediate- or short-acting agents for exacerbations.
- When possible, eliminate contributing factors (e.g., medical causes or medications).
- Change the opioid dose or agent.
- Add a psychostimulant (e.g., methylphenidate).
- Consider referral to an anesthesia pain specialist.

A separate study did show that about one-third of cancer patients on opioids had possible or definite cognitive impairments. The largest risk factor was a very high opioid daily dose. Patients taking 400 mg or more of oral morphine equivalents daily had a 1.75 times higher chance of having cognitive impairment (as measured by the Mini Mental State Examination score <27) than those taking daily equivalent doses of 80 mg or less (Kurita et al. 2011). No opioid was more or less problematic than another. Other risk factors for patients on opioids included older age, poorer Karnovsky Performance status, less than 15 months since cancer diagnosis, as well as no breakthrough pain. The lack of breakthrough pain leads me to wonder whether the baseline opioid dose these patients were taking was a little too high, and whether that contributed to their cognitive problems.

Unless local statutes or state legislation prohibit it, the evidence suggests that patients with a good performance status, who are not elderly, and who are taking a stable dose of chronic opioids of less than 400 mg morphine equivalent should be allowed to continue driving. They should be cautioned, however, not to drive if they feel sedated, if they have taken alcohol or other sedating medications, or, as noted above, for a week or two after beginning opioids or after an increase in opioid dose. Given that the states vary in their regulations about driving while taking any form of opioid for any length of time, it is important to caution your patients about their potential risk should they choose to drive or operate other motorized vehicles, and to document that you have counseled them.

In some patients, what may look like excessive sleepiness is simply a natural effect of pain relief in someone who has been sleep deprived. Patients who have just begun opioid treatment often have experienced days to weeks of severe to excruciating pain before coming to see you, and the pain has deprived them of much-needed sleep. Be careful not to mistake this natural "catch-up" sleep as oversedation. Leave the opioid dose the same for the first few days, and if the patient then complains of excessive drowsiness, with good pain relief, lower it.

Prescribe both immediate- and sustained-release formulations. A simple way to minimize sedation is to use long-acting or sustained-release opioids (i.e., methadone, transdermal fentanyl, or the sustained-release opioid preparations) that have lower peak opioid levels to deliver the majority of the pain relief. Since sustained-release preparations are not flexible enough to meet the patient's changing pain needs, however, you will usually need to use both a sustained-release preparation to keep the pain at a satisfactory level most of the time and an immediate-acting agent for rescue dosing.

Contributing causes. If sedation persists beyond the first few weeks, the sedation is not acceptable, and the patient's care is not focused solely on comfort,

try to determine whether a new medical problem, like hypercalcemia or hyponatremia or an unsuspected brain metastasis or a subdural hematoma, is contributing to the somnolence. Hyperglycemia, if it is causing sedation, is usually clinically apparent, as are uremia or hepatic failure, which also are likely to exacerbate the sedating effects of opioids.

In immunocompromised patients, search for CNS infections, such as viral encephalitis, toxoplasmosis, or tuberculous or cryptococcal meningitis. Carcinomatous or lymphomatous meningitis usually manifests as headaches and cranial nerve abnormalities rather than sedation.

If none of these conditions is present, review the patient's other medications, because a number of them can exacerbate opioid-induced sedation. Cimetidine, anticholinergic drugs, alcohol, and drugs that decrease glomerular filtration, such as NSAIDs and some ACE (angiotensin-converting enzyme) inhibitors, all increase drowsiness in patients taking opioids. Sleep medications are most often implicated.

Benzodiazepines with long half-lives, such as clonazepam (e.g., Klonopin) or diazepam (e.g., Valium), may induce daytime somnolence in patients taking opioids. To minimize daytime sedation, use zolpidem (Ambien) (5 to 10 mg p.o.) or trazodone (25 to 50 mg p.o. initial dose) for sleep. If you use a benzodiazepine during the day, choose one with a shorter half-life, such as oxazepam (e.g., Serax) (15 to 30 mg p.o.), lorazepam (e.g., Ativan) (1 mg p.o.), or temazepam (e.g., Restoril) (7.5 to 30 mg p.o.).

Change the opioid dose or the agent. If sedation persists when the contributing factors are eliminated, try decreasing the dose of the sustained-release opioid by 10 to 25 percent and monitoring the patient's use of rescue medication. If the patient doesn't use more rescue doses, you can assume the pain relief is still satisfactory.

Alternatively, substitute a different opioid agent at an equianalgesic dose (I discuss how to do this later in the chapter). Just as opioids differ in how often they induce nausea, morphine, hydromorphone, fentanyl, and the other agents differ in the frequency with which they induce sedation. You may be able to achieve equivalent pain relief with less sedation simply by using a different agent.

Psychostimulants. If none of these measures is successful, consider adding a psychostimulant, such as an amphetamine. Some effective psychostimulants and their usual starting doses are listed in Table 6.8. Amphetamines have been shown to reduce drowsiness and to enhance mood. They are contraindicated for patients with arrhythmias, delirium, or psychosis, and some patients cannot tolerate either the cardiac or the psychological side effects after starting the drugs. Even patients who can tolerate these agents may need an increased

dose to maintain their antisedating and mood-enhancing effects after three to four weeks.

For selected patients, psychostimulants can be very effective, and the benefits can persist for 6 months or more. I most often prescribe methylphenidate (e.g., Ritalin). It is a CNS stimulant that increases concentrations of dopamine at the synapse by preventing its reuptake, affects norepinephrine reuptake, and binds to the serotonin transporter. Its effects peak 2 hours after it is taken, and the immediate-release form lasts up to 6 hours. The oral sustained-release formulation has its peak effect 4 to 7 hours after it is taken and lasts approximately 8 hours and a transdermal patch is also available.

There have not been any large randomized and controlled trials that demonstrate the effectiveness of methylphenidate in relieving the somnolence induced by opioids, but numerous trials of cancer patients with impaired cognition (e.g., with brain tumors) have demonstrated that this drug is effective and safe. Patients should begin with 2.5 to 5 mg of immediate-release methylphenidate once a day; you can add a noontime dose if necessary, and escalate to no more than 1 mg/kg/day in divided doses (Rozans et al. 2002). Modafinil (Provigil) (100 to 400 mg/day p.o.), a nonamphetamine psychostimulant, is an agent approved for treatment of patients with narcolepsy. Patients with brain tumors or with sedation from opioids may find it increases their alertness.

If a patient needs an extra degree of mental acuity for a special event, such as a wedding, an important meeting, or an anniversary party, beginning the psychostimulant a week or so before the event and adjusting its and the opioid's dose can often provide the perfect degree of pain relief and mental alertness for the important day.

Anesthesia pain specialists. If all these techniques are ineffective and the patient remains unacceptably sedated, you might consider referring her to an anesthesia pain specialist, whose contributions I discuss elsewhere in the chapter.

Opioid Overdose

Sadly, an opioid overdose may result when a patient attempts to commit suicide by taking more than the prescribed dose. But inadvertent overdoses are much more common than intentional ones. Patients may take the sustained-release preparation when they intended to take the immediate-release version of the same opioid. Or they may develop renal or hepatic insufficiency that is significant enough to prolong the half-life of the opioid. Patients may place new fentanyl patches without removing the old ones or can develop toxicity if they become febrile (which increases fentanyl's absorption from the skin reservoir) or septic

(because acidosis increases the free fraction of fentanyl). Rarely, within hours of taking a significant dose of a sustained-release opioid, a patient may develop a bowel obstruction or other bowel catastrophe causing ileus; the opioid cannot be excreted in the usual fashion, and much more than the expected amount is absorbed, leading to an overdose. In any of these situations, family members may mistakenly ascribe the increased sedation to progressive cancer or to an expected side effect of the medication.

Diagnosis. Signs of opioid overdose in cancer patients are similar to those in patients without cancer, except that miosis in a patient who is opioid tolerant is not specifically indicative of overdose, and sedation may be more prominent than respiratory depression if the overdose is caught early. Assess for the causes listed above, particularly for any "extra" fentanyl patches.

Management. Patients with cancer who overdose but who have been taking opioids for chronic cancer pain cannot be managed in the same way as those who have been using opioids for only a brief time, such as previously opioid-naïve postoperative patients (Boyer 2012). It is very important even in this situation that you *resist* the temptation to use an undiluted injection of naloxone to reverse the effects of the opioid completely. If you do administer undiluted naloxone to a patient who is opioid tolerant and who has been using chronic opioids for pain control, you may precipitate a severe withdrawal syndrome, causing the patient to wake up in excruciating pain that you will have a very hard time bringing under control, even if you reinstitute opioids.

If the patient is breathing normally but cannot be aroused, simply discontinue the opioid. If significant respiratory depression has occurred, you will need to administer a dilute solution of naloxone. The low dose of naloxone enables the patient to reestablish normal respirations and wake up gradually without experiencing withdrawal.

Dilute naloxone can be given as either a slow intravenous "push" or a continuous infusion. For patients whose respiratory rates are between 10/min and 12/min, who are just mildly oversedated, and whose renal, hepatic, or gut function can be expected to normalize quickly, I suggest the following: dilute the 1 ml containing 0.4 mg of naloxone into 10 ml of normal saline, then infuse as much of this dilute naloxone as is necessary to establish a normal respiratory rate but not enough to awaken the patient. The dose can be repeated as needed.

Then, for patients whose opioid levels are likely to be elevated for a prolonged period, begin an intravenous infusion of naloxone and adjust the rate so that normal respirations are established but the patient does not wake up suddenly. Patients who have developed toxic effects from the fentanyl from a transdermal fentanyl patch, and those who have been taking sustained-release morphine or

oxycodone and develop hepatic or renal failure or an ileus, are likely to require naloxone drips. These patients should be admitted to an intensive care unit (Boyer 2012). The patient with an intrathecal pump can pose a particularly difficult problem if the pump was overfilled or incorrectly programmed. Such a patient may require lavage of the CSF as well as the naloxone to recover (Boyer 2012).

In addition to the naloxone drip, it is wise to institute measures that will stop the patient from aspirating and from absorbing additional amounts of the opioid. Gastrointestinal decontamination with activated charcoal can be used if the ingestion occurred no more than one hour before the patient arrived in the emergency department (Boyer 2012). Laxatives, oral or intravenous motility agents (e.g., metoclopramide), and enemas all help the patient eliminate the remaining sustained-release opioid from the gastrointestinal tract. Unfortunately, as mentioned earlier in this chapter, even after the transdermal fentanyl patch is removed, the patient will be absorbing fentanyl from the skin reservoir for 12 to 24 more hours. As the patient begins to wake up, reduce the naloxone infusion gradually to match the residual opioid level. Patients will awaken safely, without withdrawal; as pain reappears, appropriate opioid therapy can be resumed.

Opioid Neurotoxicity

Opioid neurotoxicity is an unfortunate complication of our eagerness to relieve a patient's pain quickly, especially when the patient is dying and the focus is on comfort. With rapidly escalating doses, a number of complications may arise (Moryl et al. 2008).

Myoclonic jerking (multifocal myoclonus) is one of the earliest and most common manifestations. It can be seen in patients taking high doses of any opioid but is most common in patients receiving frequent, repeated therapeutic doses of morphine or high doses of hydromorphone. In its earliest stages, patients experience muscle jerking as they are falling asleep. With increasing opioid doses, family members or patients themselves may report muscle spasms or involuntary movements while the patient is awake. The spasms may be severe enough to exacerbate the distress from an already painful limb. Patients receiving moderate to high doses of other opioids who develop renal insufficiency or dehydration may develop myoclonus, possibly related to increased levels of opioids and their metabolites. If nothing is done, seizures may result.

Changing to another opioid often relieves the problem. If the patient would prefer not to change opioids, benzodiazepines, baclofen or dantrolene can reduce the spasms. For patients with severe myoclonus or for those too close to dying for a trial of opioid rotation, midazolam may be particularly effective. Rarely,

patients can either be resistant to a benzodiazepine or have a history of increased agitation after receiving one. For these patients, I use a barbiturate infusion, usually with pentobarbital, to sedate them until the other measures reduce the myoclonus. In Chapter 10, I review how to give midazolam or pentobarbital.

Hyperalgesia is often even more distressing than myoclonus. It is caused by "wind-up" of the central nervous system, with spreading of the pain signals throughout the spinal cord, so that when once an arm was painful, now any limb can cause pain when moved. Even softly touching the skin can be painful for the patient, because the A-alpha (touch) fibers now act as C (pain) fibers, and transmit a painful signal.

The treatment for hyperalgesia is to lower the opioid dose rapidly, and perhaps, if it is feasible in a dehydrated patient, to give a liter or two of intravenous fluids to flush out the opioid metabolites. Ketamine, starting at 0.02 to 0.05 mg/kg per hour by continuous intravenous infusion and titrated as needed, as rapidly as 100 percent every 4 to 6 hours (Moryl et al. 2008), can provide pain relief while the opioid levels fall, but other patients may need mild sedation with a benzodiazepine. It can be very difficult, but of course crucial, to explain to the patient's family why you are decreasing or stopping the opioids when the patient seems to be in such distress.

If the patient is expected to live long enough, rotate to another opioid. Start with a dose of opioid that is equivalent to the dose the patient previously tolerated without toxicity. For example, Sylvia was a 60-year-old woman who was dying at home of multiple myeloma but was not in a hospice program because she needed platelet transfusions twice a week. She had been receiving hydromorphone via a PCA with a basal infusion of 4 mg/hr. As we unraveled the story later, she had begun to moan, likely because she had developed a mild delirium, and her family had misunderstood the moans as pain and repeatedly asked the home care nurse to increase the basal rate of the hydromorphone infusion. Over the next 48 hours, the drip rate had been increased to 16 mg/hr, and Sylvia had developed painful myoclonus and hyperalgesia. When she was admitted, she was dehydrated, so we hydrated her, then lowered the hydromorphone infusion to 4 mg/hr. We added midazolam, which quickly eliminated her myoclonus, and used low doses of liquid methadone (2 mg p.o.) to treat the increase in pain we expected her to have when the aides bathed her or changed her position in bed. We later rotated her to oral methadone, using as the base of the calculation the 96 mg a day of hydromorphone she received from her 4 mg/hr hydromorphone drip. (Earlier in the chapter, under the discussion of methadone, I describe how to do the rotation from another opioid to methadone.)

Delirium

Delirium can be a frightening side effect for both patients and their families. The first manifestation may be something as mild as nightmares, but the process can rapidly progress, and the patient can develop hallucinations and even frank psychosis.

As reviewed in Chapter 5, delirium from all causes shares the same manifestations: agitation, hallucinations, paranoid ideation, disordered thinking and perception, delusions, labile mood, and what is termed "psychomotor behavior"—picking at bed sheets, for example. Even delirious patients who seem withdrawn share the same mental disturbances as those who appear agitated. To make the diagnosis early, ask patients on opioids routinely whether they have begun having nightmares or delusions. If they have, lower the opioid dose if you can without impairing pain relief. If pain returns, switch them to another opioid.

The cause of the delirium induced by opioids is not known, but it is unusual for a full-blown delirium to be due to an opioid alone. Contributing factors include structural brain lesions, vascular or alcohol-induced brain atrophy, dementias, hypoxia, metabolic abnormalities such as renal or hepatic failure, electrolyte imbalance, nutritional deficiency (especially of B vitamins), infections, and drugs.

Drug-induced delirium. Drugs other than opioids and psychostimulants can induce delirium. Corticosteroids can cause delirium either immediately or weeks to months after they are instituted. Benzodiazepines, particularly lorazepam (e.g., Ativan), can paradoxically cause extreme agitation or delirium.

PRACTICE POINTS: MANAGING DELIRIUM (PART 1)

- Change the opioid or lower the dose.
- Evaluate appropriate patients for contributing medical conditions (e.g., brain lesions, electrolyte imbalance, hypoxia, infection, nutritional deficiency, renal or hepatic dysfunction).
- Discontinue contributing medications (e.g., acyclovir, amphotericin B, anticholinergics or agents with anticholinergic side effects, antiemetics, psychostimulants, short-acting benzodiazepines, steroids).
- Review the recent antineoplastic drug regimen for contributing agents (e.g., asparaginase, bleomycin, carmustine, cisplatin, cytosine arabinoside, etoposide, 5-fluorouracil, hexylmethylmelamine, ifosfamide, interferon, interleukin-2, methotrexate [high-dose], procarbazine, vinblastine, vincristine).

Anticholinergic agents (H_2 blockers [e.g., cimetidine] and tricyclic antidepressants), especially when combined with drugs that have anticholinergic side effects (such as diphenhydramine [e.g., Benadryl] or hydroxyzine [e.g., Atarax, Vistaril]), can cause a "cholinergic crisis," a life-threatening syndrome that includes high fevers and delirium.

Both anticholinergic crisis and serotonin syndrome can be induced by a combination of drugs commonly used to support cancer patients. Each can present as delirium, and they are both difficult to recognize, but each is life-threatening if not caught early and treated aggressively.

Identifying the Cause of Delirium: Anticholinergic Crisis

Mr. Martinez was a patient with metastatic pancreatic cancer. His family complained to his oncologist, Dr. Greenleaf, that his pain medications were "making him act funny." They wanted them stopped. Over the past week, they said, he had become intermittently confused and agitated. He occasionally appeared to be having hallucinations, and he sometimes accused his family of being "out to get him." Dr. Greenleaf suspected another cause, because Mr. Martinez's opioid regimen had not been changed in many weeks; his pain was still well controlled by a 100 µg/hr Duragesic (transdermal fentanyl) patch, along with twice daily Dilaudid (hydromorphone) for rescue.

Dr. Greenleaf evaluated Mr. Martinez and thought he might be becoming delirious. She agreed with the family that the fentanyl and hydromorphone might be contributing but explained that Mr. Martinez needed opioids of some type to control his pain and wanted to admit him to the hospital to evaluate him for other causes. She asked me to recommend several agents that she could safely prescribe, contacted Dr. Blair, a psychiatrist, and admitted Mr. Martinez for evaluation and therapy.

In response to my questions about what other medications Mr. Martinez was taking, Dr. Greenleaf told me that Mr. Martinez, like many patients with pancreatic cancer, was depressed, and that for four months before this incident, he had been taking amitriptyline. His response to the amitriptyline had been excellent: his mood was much improved and he was getting much more pleasure out of life. Two weeks before the admission, Dr. Greenleaf had added cimetidine and hydroxyzine (Atarax) for new gastritis and severe pruritus due to increasing biliary obstruction. His family confirmed that Mr. Martinez had been taking most of these medications as prescribed, but that one week prior to his change in behavior, he had doubled his hydroxyzine dose when his pruritus worsened.

Given this new information, I thought it was less likely that the opioids were causing Mr. Martinez's delirium than that the combination of amitriptyline,

cimetidine, and an increased dose of hydroxyzine had precipitated a *cholinergic crisis* manifesting as delirium.

Dr. Blair agreed. On our recommendation, Dr. Greenleaf discontinued cimetidine and hydroxyzine, added omeprazole for gastritis and cholestyramine for the bile acid–induced pruritis, and substituted a different opioid, intravenous morphine, for pain management. Because Mr. Martinez had not developed the crisis when taking amitriptyline and opioids alone, and because amitriptyline had been of significant benefit, we thought it could safely be continued. Dr. Blair suggested haloperidol (Haldol) to control Mr. Martinez's agitation and disordered mentation. Ten days later Mr. Martinez's mental status had greatly improved, and he no longer required haloperidol. Because we could not be sure the fentanyl and hydromorphone had not contributed to the delirium, I advised Dr. Greenleaf to convert the intravenous morphine drip to oral sustained-release morphine and immediate-release oral morphine for rescue.

We explained to Mr. Martinez and his family why the delirium had developed and why it was safe for him to continue taking opioids and amitriptyline. On this regimen, he was able to maintain excellent symptom control without recurrence of a cholinergic crisis until his death two months later.

Identifying the Cause of Delirium: Serotonin Syndrome

Angela Forsythe was a 64-year-old woman with recurrent glioblastoma multiforme, who was being treated with dexamethasone and a fentanyl patch of 25 mcg/hr to control her headaches. She was also taking citalopram for depression and had been doing well.

Angela came in for a routine visit during which her oncologist, Dr. Wang, reviewed the results of her MRI, which showed stable disease, and he introduced the idea of home hospice care. Angela complained of oral pain and difficulty swallowing. Dr. Wang diagnosed oral and esophageal thrush and began a course of fluconazole. A week later, Angela's daughter called our palliative care program nurse because of a change in her mother's condition. Her arm and leg muscles seemed to be jumping for no reason, and she was much more confused and didn't respond to questions. We urged Angela's daughter to bring her mother to the hospital.

In the Emergency Department, Angela was confused and had severe cognitive deficits, especially with memory; a flat affect; and periods of "absence," when she wouldn't respond to questions. She had mild myoclonus and hyperreflexia, tachycardia, and tachypnea. Her repeat MRI showed no change from the previous week, and there were no new metabolic abnormalities. Her only new medication was the fluconazole.

After Angela was admitted to the hospital, serotonin syndrome was confirmed as the likely etiology of her symptoms. Her family revealed that Angela had begun

to develop the change in her behavior about three days after the fluconazole was started, and an EEG done after admission showed nonconvulsive seizure activity, responsive to lorazepam. The citalopram was discontinued, lorazepam was used for anxiety and myoclonus, and her mental status returned to its prior state within a few days.

Serotonin syndrome can be caused by an overdose of an SSRI (selective serotonin reuptake inhibitor). But more typically in patients who have cancer, it is caused by adding an agent that inhibits the metabolism of the SSRI, causing an increase in SSRI blood levels. SSRIs are metabolized in the liver by CYP2C19 and 3A4, so inhibitors of these cytochromes, like fluconazole, can easily cause the syndrome (Table 6.9).

The typical findings of serotonin syndrome include (Levin et al. 2008, p. 374):

1. Neuromuscular hyperactivity; tremor, clonus, myoclonus, hyperreflexia, and, in the advanced stage, pyramidal rigidity.
2. Autonomic hyperactivity: diaphoresis, fever, tachycardia, tachypnea and mydriasis
3. Altered mental status: agitation and confusion in advanced stages.

Angela had many, but not all, of these findings. Her dexamethasone prevented the diaphoresis and fever, and the fentanyl prevented mydriasis. Had she been receiving lorazepam for anxiety, she would not have had myoclonus, either. She was fortunate that her clinicians had a high degree of suspicion and were able to confirm her diagnosis and treat her promptly, so that she recovered to her baseline.

PRACTICE POINTS: MANAGING DELIRIUM (PART 2)

- Obtain a psychiatric consultation for all patients with delirium.
- Begin therapy directed at reversing the underlying etiologies whenever possible.
- Surround the patient with the familiar (people, objects, and sounds).
- Frequently reorient the patient to place, day, date, and time.
- Give haloperidol, 0.5 to 1.0 mg IV or 1 to 2 mg p.o., and repeat q6h with 1 to 2 mg q2h p.r.n. until either the agitation resolves or 20 mg has been given within 24 hours.
- For refractory patients who can take oral medication, give olanzapine, 2.5 to 5 mg p.o. b.i.d., and 2.5 mg q4h p.r.n.
- For very agitated patients, consider adding lorazepam (0.5 to 1 mg).

Therapy for delirium. Whenever possible, consult a psychiatrist for patients with delirium, and when the patient's condition permits, initiate treatment for the underlying cause. It is fortunate that the initial episode of delirium reverses in 50 percent of patients, even when the cause remains unknown (see Table 6.9). Subsequent episodes reverse only 25 percent of the time (Lawlor et al. 2000). Dr. Eduardo Bruera, a noted hospice physician, educator, and researcher, was able to identify an etiology for the delirium in only half of his terminally ill patients. But he and others have identified some simple but effective measures to help these patients:

- Ask a nurse, friend, or family member to sit with the patient to decrease her anxiety and help with orientation.
- Move the patient to a well-known favorite room.
- Leave a night light on.
- Put a clock and a calendar within sight, along with favorite, familiar objects (Breitbart 2010).

If these techniques do not work, pharmacologic therapy often does. Haloperidol (1 to 4 mg p.o. at bedtime or b.i.d. to t.i.d. and every 4 hours p.r.n.), a butyrophenone, will diminish the patient's agitation, clear her sensorium, and improve her ability to think clearly. If it needs to be given parenterally, start with or 0.5 to 1 mg IV two to four times daily, because the parenteral dose is approximately twice as strong as the oral dose. Do not exceed doses of 20 mg in 24 hours to avoid inducing the often fatal neuroleptic malignant syndrome (NMS), which presents with rigidity, high fever, encephalopathy, and widely fluctuating pulse and blood pressure (Caroff et al. 2011). When the patient's delirium comes under control, continue the haloperidol at the same dose and frequency that was effective, and then taper it over several weeks, as tolerated. The patient's mental status may not return to normal for several days, but her agitation and fear usually resolve within one or two days.

If the haloperidol is not effective and the patient can take oral medications, discontinue the haloperidol and start olanzapine (Zyprexa, Zydis) (2.5 to 5 mg p.o. b.i.d. plus 2.5 mg p.o. every 4 hours p.r.n.).

If patients develop akathisia from these agents, discontinue them and start a beta blocker: oral propranolol (40 mg orally t.i.d.) or intravenous metoprolol at an equivalent dose (Avital et al. 2009). Zolmitriptan 7.5 mg orally daily, in a double-blind comparative study (Avital et al. 2009), and mirtazapine (15 mg p.o. daily), in a double-blind placebo and propranolol-controlled trial (Poyurovsky et al. 2006), have also shown efficacy comparable to propranolol in reversing

the akathisia, but patients in the Poyurovsky study were given only 40 to 80 mg of propranolol daily.

The atypical antipsychotic aripiprazole (Abilify) is also effective (5 mg p.o. daily; may increase as needed to a maximum of 30 mg). Strong CYP3A4 inhibitors like fluconazole may greatly increase serum concentrations of aripiprazole, and it is important to reduce aripiprazole doses by half in patients who receive both agents. The advantage of aripiprazole over haloperidol is the lower incidence of extrapyramidal symptoms (FDA 2003), especially at doses of haloperidol needed by patients with hyperactive delirium (Boettger et al. 2011), and the lack of prolongation and perhaps even reduction of the QTc interval (Goodnick and Jerry 2002; FDA 2003).

All three agents (i.e., haloperidol, olanzapine, and aripriprazole) are effective for patients with either hypoactive or hyperactive delirium. If the delirium was induced by corticosteroids, opioids, or metabolic abnormalities (e.g., hypercalcemia), treat the delirium while you are trying to reverse the underlying cause; the patient is likely to respond even though the precipitating cause is still present.

For patients refractory to these agents, chlorpromazine (e.g., Thorazine) (25 to 100 mg p.o., IV, or p.r. b.i.d. to q.i.d.) is effective. Chlorpromazine induces orthostatic hypotension, and is more sedating and has a higher incidence of anticholinergic and cardiovascular side effects than haloperidol. Chlorpromazine is particularly helpful for patients with terminal delirium who are not getting out of bed, and in whom the sedation is usually an acceptable price to pay for control of the delirium.

For some patients experiencing a particularly agitated delirium, whose agitation remains despite therapeutic doses of haloperidol, adding lorazepam to the haloperidol may be helpful. Oral, rectal, or parenteral lorazepam (e.g., Ativan) is used in doses of 0.5 to 1.0 mg every 2 hours. It can be given to patients with renal or hepatic impairment, is relatively inexpensive, and in the parenteral form is 80 percent bioavailable when given rectally. The parenteral form of diazepam (e.g., Valium) is also well absorbed rectally. Unfortunately, studies show that more than half of patients treated with rectal diazepam experienced a sensation of rectal burning lasting up to 15 minutes (Warren 1996). Clonazepam has been shown to be absorbed rapidly from the rectum in normal adults, so it, too, can be considered in treating agitation.

The treatment of delirious patients who are actively dying is reviewed in Chapter 10. Home hospice teams can administer medications that help both the patient and the family find peace during the patient's last days.

Respiratory Depression

Respiratory depression is a very unusual side effect when opioids are used to treat cancer patients in pain, as long as the opioid dose is titrated to the degree of pain, and the patient's renal and hepatic functions remain stable (Legrand et al. 2004). Opioids do marginally decrease the brain's sensitivity to carbon dioxide levels and are associated with a slight, usually clinically insignificant, degree of hypoventilation.

It is sometimes difficult to determine whether a patient's respiratory depression is due to the opioid or to something else. If an opioid is responsible, the patient will also be confused and somnolent, because opioid-induced respiratory depression is due to general depression of the central nervous system. If the patient is anxious or agitated, however, something other than opioids must be causing the respiratory depression.

PRACTICE POINTS: MANAGING OPIOID-RELATED RESPIRATORY DEPRESSION

- Respiratory depression in an agitated patient is unlikely to be due to the opioid.
- Respiratory depression may indicate worsening of renal or hepatic function, hypothyroidism, persistence of drug in the bowel because of obstruction, or sepsis.
- Induce evacuation of residual opioid from the gut and remove any opioid-containing skin patches.
- If respiratory rate is dangerously low, infuse a dilute solution of naloxone until the rate returns to a safe level. Do not give enough to awaken the patient or to induce opioid withdrawal.

Occasionally, patients have underlying medical conditions that make them more susceptible to the respiratory depressive effects of opioids. Hypothyroid patients or those whose obstructive lung disease causes them to retain carbon dioxide are in this category. Hypothyroid patients with coronary artery disease and angina can be particularly problematic; they can develop respiratory arrest with even the 1 or 2 mg of morphine they receive for pain in the emergency room. For patients with chronic obstructive pulmonary disease, you can safely prescribe opioids if you start with very low concentrations (e.g., morphine 0.25 mg/hr), increase the doses very slowly, and monitor the patient carefully.

Miscellaneous Side Effects

Opioid-induced *urinary retention* is also troublesome, especially for older patients or those with underlying bladder outlet obstruction. Discontinuing any agents with anticholinergic side effects is often effective, but some patients may require finasteride (e.g., Proscar) (5 mg/day p.o.) to diminish the outlet obstruction, or bethanechol (e.g., Urecholine) (10 mg p.o. t.i.d., to a maximum of 50 mg p.o. t.i.d.) to relax the bladder smooth muscle that is being stimulated by the opioid.

Pruritus, which most commonly occurs in opioid-naive patients receiving epidural or intrathecal opioids, may be caused by activation of spinal opiate receptors, by opioid-induced release of histamine from mast cells, or by disinhibition of itch-specific neurons (McNicol et al. 2003). Pruritus may resolve with a change in opioid, but you may need to add ondansetron (4 mg p.o. or IV); paroxetine (Paxil) (10 to 20 mg p.o.) (Zylicz et al. 1998); nalmefene (10 to 25 μg IV); or nalbuphine (1 to 5 mg IV) (Hough et al. 2003). General strategies for treating pruritis can be found in Chapter 9.

Summary

Constipation, nausea, sedation, opioid neurotoxicity, delirium, respiratory depression, urinary retention, and pruritus are treatable opioid-induced side effects that can often be prevented. They can discourage patients from taking the doses of opioids they need to achieve satisfactory control of their pain. For patients with complicated pain syndromes, you may need to prescribe a number of agents to prevent or control side effects, and the patient may need to try two or three different opioids before achieving satisfactory pain control with tolerable side effects. By using these strategies you will be able to reverse or ameliorate those problems that do occur and markedly increase the comfort of your patients.

Adjuvant Analgesic Treatments

Adjuvant analgesics are drugs used primarily for other indications that also produce pain relief. They are of particular value for patients with neuropathic pain, including patients with spinal cord compression (see Tables 6.10) or bone pain (see Table 6.11). In the sections that follow, I describe how to use various adjuvant analgesics for the treatment of neuropathic pain, including corticosteroids, anticonvulsants, and psychotropics. I also review agents useful for bone pain, and then discuss neuroleptics, skeletal muscle relaxants, and smooth muscle relaxants.

Adjuvant analgesic agents are usually given orally or parenterally, but occasionally rectal administration is preferable. Unfortunately, though there is good information about the rectal use of opioids and NSAIDs, we have less information about administering adjuvant medications via this route.

Adjuvant Treatments for Neuropathic Pain

Opioids can relieve both central and peripheral neuropathic pain syndromes (Rowbotham et al. 2003), but other than methadone (discussed earlier in this chapter), the side effects of the opioids can limit the doses that are tolerable. Patients with neuropathic pain usually need to take adjuvant agents that can block the pain produced by the damaged nerve.

When a peripheral nerve is injured, inflammatory mediators are released that cause changes in the sodium channel activity of the nerves at that site and at the dorsal root ganglion, and new calcium channels appear. These changes cause "peripheral sensitization," which is both a lowering of the threshold for nerve firing and a spontaneous firing of the nerves. Unlike opioids, drugs that can modify the ion channels—such as corticosteroids, gabapentin, pregabalin, and the other anticonvulsants; serotonin norepinephrine reuptake inhibitors; tricyclic antidepressants; local anesthetics; and clonidine (see Table 6.10)—can provide the extra analgesia needed for satisfactory relief of the discomfort that comes from peripheral and central sensitization (Beydoun and Backonja 2003; Dworkin et al. 2007; Attal et al. 2010).

Acute chemotherapy-induced pain syndrome. Paclitaxel causes a unique acute pain syndrome that occurs in 58 percent of patients receiving the drug. The syndrome is caused by damage to peripheral nerves (not muscles or joints) and is more common if the drug is infused over 3 hours (25 percent incidence) than over 96 hours (2 percent incidence). Patients with this syndrome complain of joint and muscle aching and dull pains 1 to 3 days after each dose, and the symptoms usually resolve within a week (Loprinzi et al. 2011). The intensity of the pain predicts how severe the peripheral neuropathy is likely to be (see below).

Oxaliplatin causes a different type of acute neurotoxicity that presents as a short-lived but intense paresthesia in the throat, mouth, face, and hands; jaw spasms; and cramps triggered by exposure to cold. The pain syndrome is likely due to injury to the nerve's sodium channels (Durand et al. 2012). The SNRI (serotonin norepinephrine reuptake inhibitor) venlafaxine (150–225 mg/day), which in addition to its SNRI activity blocks activation of the sodium channel, has been shown in a phase III randomized placebo-controlled trial both to pre-

vent the acute neurotoxicity induced by oxaliplatin and to decrease the severity of subsequent chronic peripheral neuropathy (Durand et al. 2012).

In early pilot data, another SNRI, duloxetine (60–120 mg/day) has also been effective in ameliorating oxaliplatin- or paclitaxel-induced peripheral neuropathy (Matsuoka et al. 2012; Yang et al. 2012). I would give duloxetine a try if other agents haven't been effective as we await confirmation in larger studies. These SNRIs are not without side effects; common ones include gastrointestinal intolerance (dry mouth, nausea, constipation, diarrhea) as well as somnolence, dizziness, and increased sweating. Rarely, they are hepatotoxic.

Chronic chemotherapy-induced pain syndromes. Microtubule inhibitors (such as vincristine and vinblastine), taxanes, proteosome inhibitors (such as bortezomib), thalidomide, and platin-containing agents (such as cis-platin, carboplatin, and oxaliplatin) all induce peripheral neuropathies by injuring nerves in different ways (Grisold et al. 2012). Almost all patients experience numbness and tingling, and about half report burning pains that are dose related and caused by often irreversible nerve damage. Sensory loss can be so severe that it includes loss of proprioception and results in ataxia and problems walking. Symptoms lessen with time off the agents, but they and the associated functional impairments rarely resolve completely.

These chemotherapy agents induce *central sensitization*: changes in the spinal cord that occur after peripheral nerve injury. Substance P and neurokinin A released into the spinal cord by injured peripheral nerves cause changes in the activity of the calcium channels and a lowering of the threshold for firing of spinal cord neurons. These neurons also begin to respond not only to signals from the nerves that enter at their level of the cord but also to signals from nerves synapsing above and below them. In addition, more spinal cord NMDA receptors appear. These receptors inhibit the ability of opioids to relieve pain. Given all these changes, patients with central sensitization usually need treatment with agents (discussed individually later in this chapter) that affect the activity of calcium channels (such as gabapentin, pregabalin, and dantrolene) and may need agents that affect the activity of the sodium channels (such as corticosteroids or tricyclic antidepressants) or that can inhibit the activity of the NMDA receptors (such as methadone or ketamine).

Corticosteroids. Corticosteroids are effective both for patients with malignant bone pain and for those with malignant neuropathic pain, such as that caused by compression of the spinal cord or nerve plexi (e.g., brachial plexus, lumbosacral plexus) by tumor. By inhibiting synthesis of prostaglandins and by their effect on the sodium channel that decreases firing from injured nerves, corticosteroids diminish transmission of the pain signal from the periphery to

the spinal cord or from the spinal cord to the brain. By decreasing capillary permeability, they reduce edema and thereby relieve the pain of brain metastases or tumor infiltration of nerves or nerve roots. There are also clinical reports of corticosteroids relieving esophageal or gastroduodenal obstruction, but no controlled studies have been done to confirm their efficacy in these conditions.

Corticosteroids can be given epidurally, intravenously, or orally. Epidural corticosteroids have been studied only in patients with nonmalignant pain syndromes, but their success in some patients with radiculopathies (e.g., from disk disease) suggests that they might be beneficial as adjuncts for those with malignant epidural disease who cannot tolerate systemic corticosteroid therapy.

PRACTICE POINTS: CORTICOSTEROIDS AS ADJUVANTS

- Corticosteroids decrease pain due to peripheral nerve injury (e.g., acute herpes zoster or metastases to the brachial or lumbosacral plexus), spinal cord compression, and brain metastases.
- Corticosteroids also decrease bone pain.
- Onset of pain relief is often rapid.
- To minimize side effects:
  - —Give the minimal effective dose.
  - —Consider prophylaxis for oral and esophageal candidiasis and for gastritis/ulcer disease.
- Be alert for mood changes (euphoria or depression) and delirium.

Corticosteroid therapy is indicated for all patients with radiologic evidence of cord compression. Corticosteroids decrease cord edema and pain and help preserve neurologic function and overall outcome after specific therapy (i.e., radiation, surgery, or surgery followed by radiation). Intravenous corticosteroids can induce very rapid pain relief. Patients who receive high doses of intravenous corticosteroids for cord compression, for example, often experience a significant decrease of back pain within hours. There is controversy, however, about the dose that should be used. For patients with true cord compression (not just epidural tumor extension) treated with radiotherapy, high-dose dexamethasone (100 mg IV bolus followed by 24 mg p.o. q.i.d. for 3 days, then tapered over 10 days) is recommended. More patients remained ambulatory after receiving both radiotherapy and this high-dose dexamethasone than after receiving radiotherapy alone (81 percent vs. 63 percent) (Sorensen et al. 1994). (Selected patients with little epidural disease and contraindications for cortico-

steroid therapy have been shown to tolerate radiotherapy safely without corticosteroids.)

Patients usually receive lower doses of dexamethasone (10 mg IV bolus, then 4 mg p.o. q.i.d., then tapered over 14 days), but in one study these lower doses had no significant effect on patient mobility. If you choose the 100-mg dose, be sure it is given over at least 15 to 30 minutes; if given more rapidly it is likely to cause a severe, though transient, perineal burning sensation. The group of patients who received lower-dose dexamethasone remained ambulatory at the same rate as the group not given any dexamethasone (57.1 percent vs 57.9 percent) (Heimdal et al. 1992). The lower dose of dexamethasone (10 mg) does, however, provide as much pain relief as the higher dose (100 mg).

Corticosteroid therapy is also indicated as an adjuvant for all patients with radiologic evidence of cord compression while they are being evaluated for decompressive surgery. Surgery was formerly reserved for patients who had tumors that were very unlikely to respond to radiation, or whose epidural disease progressed despite radiation therapy. Data from a randomized trial suggest, however, that patients who had cancers other than lymphoma, myeloma, or breast cancer, and who were treated with surgery followed by radiation therapy, either remained ambulatory longer or were more likely to become ambulatory than patients who received radiation therapy alone (Patchell et al. 2005). If you are interested in more information about assessing and treating patients with spinal cord compression, please refer to Chapter 5 and additional references in the bibliography (Abrahm et al. 2008; Rose et al. 2009; Rades et al. 2010; Loblaw and Mitera 2011).

For patients with brain metastases or impending but not actual cord compression, consider starting with the lower-dose oral corticosteroid regimen, tapering to 4 or 2 mg every 6 hours during the second week of radiation treatments. After the radiation is completed, taper the dose as the patient tolerates. Reinstate a higher dose if back pain, headache, or other symptoms of cord or CNS edema return.

Corticosteroids are also effective adjuvants for patients with peripheral nerve injuries, such as those with tumor infiltrating the brachial plexus (typically lung or breast cancer) or the lumbosacral plexus (typically recurrent colorectal cancer). To the opioid therapy, add 4 to 6 mg of dexamethasone orally two to four times a day. In responding patients, the pain diminishes significantly by 48 to 72 hours. To minimize the corticosteroid-induced side effects, taper the dose rapidly, watching for reemergence of unacceptable pain. In many cases, patients have been able to maintain effective pain control with alternate-day corticosteroid dosing.

Antivirals have a more important role than corticosteroids in the treatment of acute herpes zoster and post-herpetic neuralgia (Thakur and Phillips 2012). Corticosteroids alone have been shown to decrease the acute pain associated with herpes zoster infections, but there is no long-term benefit, and they are not recommended as standard therapy. Adding acyclovir (800 mg five times a day for 21 days) to prednisone (60 mg/day for 7 days, 30 mg/day for the next 7 days, and 15 mg/day for the last 7 days), while leading to quicker resolution of neuritis, return to uninterrupted sleep, return to usual daily activities, and cessation of analgesics, does not prevent post-herpetic neuralgia.

Antivirals should be started within 72 hours after the patient first notices the rash. Acyclovir (800 mg, 5 times a day), valacyclovir (1000 mg, every 8 hours), and famciclovir (500 mg, every 8 hours) have comparable efficacy and safety profiles. A meta-analysis found that acyclovir decreased post-herpetic neuralgia prevalence (15 percent vs 35 percent in controls), and in other studies, famciclovir decreased its duration: 163 days in the placebo group versus 63 days in the treated group (Thakur and Phillips 2012).

Oral corticosteroids have also been used to increase patients' appetite and sense of well-being, but results of controlled studies of their efficacy have been conflicting. Increases in appetite in the short run (about one month) were consistently noted. In some studies, improvement in the amount of food eaten and patients' sense of well-being or quality of life was also seen, but neither weight nor survival time increased. The patients who showed the most improvement were those with neuropathic pain. For selected patients with advanced cancer, for whom appetite or sense of well-being is a significant issue, consider a course of corticosteroids, expecting at least a short-term benefit.

The limitation to using corticosteroids is the significant incidence of corticosteroid-induced side effects. Many of these can be prevented and others readily managed, but some of the most serious ones occur unpredictably. The corticosteroid-induced side effects and recommended treatments are described below.

Gastrointestinal Disorders. Corticosteroids alone probably do not cause ulcers. Patients taking corticosteroids along with an NSAID (other than acetaminophen), however, do have a higher incidence of ulcers than those taking the NSAID alone. Therefore, consider prescribing a proton pump inhibitor (e.g., omeprazole, 20 mg/day) for patients taking both corticosteroids and NSAIDs.

Candidiasis. One of the most common corticosteroid-induced side effects, especially in patients who are debilitated or otherwise immunocompromised, is oral or esophageal candidiasis (thrush). These conditions can be very distressing and may seriously decrease your patient's oral intake. It is therefore important

to describe carefully to the patient and his family the signs and symptoms of oral and esophageal candidal infections (the painful, burning red tongue and the esophageal pain syndrome described below). They will then be able to call you promptly and receive appropriate therapy should an infection develop.

If you plan a prolonged corticosteroid course, you might consider starting prophylactic antifungal therapy with oral fluconazole (200 mg on day one, followed by 100 mg/day). For patients expected to require only a short-term course of corticosteroids, consider oral prophylaxis with topical antifungals such as clotrimazole troches (e.g., Mycelex) given three times a day. Patients will need to be monitored for esophageal candidiasis, because these agents do not prevent it.

Esophagitis causes a very distinctive pain syndrome. Even though the infection usually involves only the lower esophagus, the pain can be experienced in the mid- or even upper esophagus. You have probably experienced esophageal pain if you have swallowed a fish bone that "got stuck" or have drunk a very hot liquid too quickly. As you may remember, a few seconds after you swallow, when the wave of peristalsis passes the injured area, the pain appears. Patients with this problem will grimace a few seconds after swallowing, when they experience the pain. You can treat esophageal candidiasis effectively with oral fluconazole; patients usually experience significant pain relief within 48 hours.

Mood Changes. Corticosteroid-induced delirium is more common in people with a previous psychiatric history, and high-dose corticosteroids should be used with caution in such patients. For most patients, the mood changes are less marked. In some, a euphoria occurs that can be quite enjoyable. The commonly associated insomnia can be prevented by instructing the patient to take the corticosteroids before noon. Other patients develop a severe corticosteroid-induced depression, which may respond to lowering the corticosteroid dose or to discontinuing it altogether. Antidepressant drugs are not usually required.

Miscellaneous. Corticosteroid-induced *glucose intolerance* is usually easily managed with insulin. For patients with impaired mental status, the visiting nurse or hospice team can be of great assistance in regulating and administering the insulin doses. Prophylaxis for pneumocystis is needed for patients on prolonged steroid therapy.

Proximal muscle weakness can be quite disabling and very refractory to therapy. Home physical therapy or, for those who can tolerate it, hydrotherapy can preserve some muscle function, but many patients will need assisting devices such as lift chairs to keep them independent in their daily activities. Others may require wheelchairs and support devices such as shower chairs.

Anticonvulsants. The anticonvulsants—gabapentin (e.g., Neurontin), pregabalin (Lyrica), phenytoin (e.g., Dilantin), carbamazepine (e.g., Tegretol), lamotrigine (Lamictal), topiramate (Topamax), and oxcarbazepine (Trileptal)—are important adjuvant agents for patients with neuropathic pain that is "burning," "sharp," "cutting," or "like an electric shock" (Table 6.10). The mechanism by which these agents relieve such pain has not yet been determined. Most of the efficacy data, other than data from studies on chemotherapy-related neuropathy, come from studies on patients without cancer who have neuropathic pain.

Gabapentin is the most commonly used agent. It has demonstrated efficacy in patients with post-herpetic neuralgia and peripheral neuropathies resulting from diabetes or chemotherapy, and is empirically used for patients with neuropathic pain of any etiology. In 2011, a new formulation of extended-release gabapentin was FDA approved for post-herpetic neuralgia (Thomas and Farquhar-Smith 2011). To minimize sedation, especially in older patients, use low doses initially and raise the dose every 3 to 4 days (or weekly in older patients) as tolerated. Start at 100 mg orally, three times a day, or, for patients with difficulty sleeping, 100 mg in the morning and evening and 300 mg at bedtime. The dose for patients with renal insufficiency is 100 to 200 mg twice a day. Give patients with renal failure who are undergoing dialysis a 300-mg loading dose, and then 200 to 300 mg after each dialysis. The minimal effective dose is usually 300 mg orally, three times a day, but if the patient reports some pain relief, the doses can be increased up to 3600 mg/day in divided doses to reduce the pain further. Sedation and peripheral edema are the usual dose-limiting side effects.

Gabapentin is well absorbed at low doses, but its bioavailability falls significantly at higher doses. The 100 mg dose has 60 percent bioavailability, but the 1600 mg dose only 27 percent. Pregabalin (Lyrica), however, is linearly absorbed at all doses, with 90 percent bioavailability and peak plasma concentration within one hour if taken on an empty stomach. Pregabalin is FDA approved for use in patients with neuropathic pain. Importantly, if a patient has suboptimal effect from gabapentin at 300 mg or more taken orally three times a day, pregabalin is likely to be effective. For pregabalin to be covered by most insurance plans, you will need to document that the patient has not responded to gabapentin.

Pregabalin has the same mechanism of action and side-effect profile as gabapentin. If you are starting someone directly on pregabalin, begin at 50 mg (p.o. t.i.d.). If the patient is already tolerant to gabapentin, the initial pregabalin dose will depend on the gabapentin dose. For example, start someone taking 300 mg (p.o. t.i.d.) of gabapentin at 50 mg (p.o. t.i.d.) of pregabalin; but start someone

PRACTICE POINTS: ADJUVANT AGENTS FOR NEUROPATHIC PAIN

- Pregabalin is the most useful anticonvulsant for neuropathic pain. It is well absorbed at all dose ranges and has the fewest side effects. Use gabapentin first if the patient cannot afford pregabalin. If gabapentin is ineffective, pregabalin may be effective; many insurers will cover its cost for patients not responding to gabapentin.
- Consider adding low-dose nortriptyline at bedtime to enhance pain relief with minimal additional side effects.
- Carbamazepine is best studied for tic douloureux–like pain, but consider giving phenytoin to achieve therapeutic levels rapidly.

taking 1200 mg (p.o. t.i.d.) at 150 mg (p.o. t.i.d.; maximum dose is 200 mg p.o. t.i.d.) (Dworkin et al. 2007; Attal et al. 2010).

If the pregabalin does not provide sufficient relief alone, try adding (in succession) lamotrigine (150 to 500 mg/day in two divided doses), topiramate (25 to 400 mg/day in two divided doses), or oxcarbazepine (300 to 2400 mg/day in two divided doses) to improve the pain control. Other active agents include divalproex (150 to 3000 mg/day in three divided doses), zonisamide (100 to 400 mg/day in two divided doses), and the benzodiazepine clonazepam (1 to 10 mg/day in two divided doses) (Farrar and Portenoy 2001; Rowbotham et al. 1998).

For patients with lancinating, electric shock–like pain that does not respond to any combination of these agents, discontinue the gabapentin or pregabalin and try phenytoin (100 to 300 mg/day) or carbamazepine (100 to 1600 mg/day, in two to four divided doses). Although carbamazepine has most often been shown to be effective, as, for example, in trigeminal neuralgia (tic douloureux), consider beginning with phenytoin. You can reach therapeutic levels of phenytoin within a day and complete a therapeutic trial in one or two weeks. If by that time the pain has not improved, discontinue the phenytoin and begin carbamazepine, increasing doses slowly (i.e., incrementally every week or two) until therapeutic levels are reached. This may take as long as a month but may help selected patients.

These other anticonvulsants cause several side effects not found in patients taking gabapentin or pregabalin, and patients on them require careful monitoring. Patients taking phenytoin may develop ataxia, nausea, vomiting, or visual problems if the dose exceeds the therapeutic range; they may also develop allergic reactions involving the skin or liver. Carbamazepine causes hypotension in ambulatory patients if the dose is escalated too rapidly, and it can (rarely)

cause severe neutropenia. Lamotrigine commonly causes fatigue, dizziness, headache, rash, mental status changes, blurred vision, nausea and vomiting, and, rarely, serious allergic skin reactions and cytopenias and hepatic failure. Begin by giving 25 mg/day orally for 2 weeks, increasing to 50 mg/day orally for 2 weeks and then to 100 mg/day orally for 1 week, as tolerated. The maximum dose is 200 mg/day orally.

Topiramate commonly causes dizziness, somnolence, fatigue, mental status changes, and depression, and, rarely, kidney stones, acute angle-closure glaucoma, oligohydrosis and hyperthermia, cytopenias, psychosis, and severe allergic skin reactions. Begin topiramate doses at 25 to 50 mg/day orally, and increase by 25 to 50 mg/day each week. Doses above 400 mg are rarely more effective than lower doses.

Oxcarbazepine commonly causes dizziness, somnolence, confusion, diplopia, fatigue, nausea, vomiting, abdominal pain, abnormal gait, nystagmus, and, rarely, severe allergic skin reactions, cytopenias, angioedema, and hyponatremia. Oxcarbazepine doses should begin at 300 mg orally twice a day and increase by 300 mg every 3 days as tolerated, to a maximum of 2400 mg/day orally.

Levetiracetam (Keppra) is particularly difficult for patients to tolerate, as it commonly causes somnolence that does not remit with continued therapy. It also commonly causes asthenia, dizziness, ataxia, agitation, anxiety, emotional lability, behavior changes, and anemia. Begin at 500 mg orally every 12 hours, for 2 weeks, and increase by 1000 mg/day every 2 weeks to a maximum of 3000 mg/day.

Serotonin norepinephrine reuptake inhibitors. Unlike SSRIs, which have no pain-relieving activity, the SNRIs venlafaxine (Effexor) (150–225 mg/day) and duloxetine (Cymbalta) (60–120 mg/day) are helpful for patients with neuropathic pain. Both are recommended (along with gabapentin and pregabalin) as first-line therapy for patients with diabetic neuropathy (Attal et al. 2010). As discussed earlier in the chapter, venlafaxine is helpful for patients receiving oxaliplatin, and duloxetine helps patients receiving either oxaliplatin or paclitaxel. The SNRIs are not without side effects; common ones include gastrointestinal intolerance (dry mouth, nausea, constipation, diarrhea) as well as somnolence, dizziness, and increased sweating. Rarely, they are hepatotoxic.

Tricyclic antidepressants. Tricyclic antidepressants (TCAs) are also effective as adjuvant analgesics for patients with neuropathic pain (see Table 6.10) (Saarto and Wiffen 2010), but their anticholinergic side effects (e.g., dry mouth, dry eyes, blurred vision, constipation, hypotension, urinary retention, and sedation) limit their usefulness. At doses far below those needed for an antidepressant effect, nortriptyline, which has the least of these side effects, is well tolerated and

effective. TCAs like nortriptyline add efficacy to therapy with gabapentin (and by inference, also pregabalin) (Attal et al. 2010; Gilron et al. 2009). Neuropathic pain is often worse at night, so give the nortriptyline at bedtime, starting at 10 mg orally.

To avoid misunderstandings, before a patient begins taking an adjuvant antidepressant, ensure he understands that just because you're using an antidepressant to treat his pain, you don't think the pain is "all in his mind."

Baclofen. Baclofen, a GABA (gamma-aminobutyric acid) antagonist, acts primarily at the spinal cord level and is normally used to relax spastic limbs of patients with CNS disease. It is also useful for cancer patients who have developed spasticity after spinal cord injury. Baclofen relieves trigeminal neuralgia pain and so may help those patients with cancer of the head and neck who develop a neuropathic pain syndrome similar to that of trigeminal neuralgia.

Baclofen is usually given orally, three times a day, but it can be given intrathecally if necessary. Oral doses begin at 5 mg three times daily and are escalated every 3 days by 5 mg at each dose to a target of 40 to 80 mg/day. This gradual dose increase minimizes the drowsiness, dizziness, hypotension, nausea, and confusion that the drug can induce. If the patient needs to discontinue baclofen, taper it gradually to prevent the patient from developing psychiatric disorders, hallucinations, or seizures.

Clonidine. Clonidine, an alpha-2-adrenergic agonist usually used to treat hypertension, is also able to relieve pain and will prevent opioid withdrawal in patients who must discontinue opioids following development of opioid bowel syndrome. Used either transdermally or in intrathecal infusions, clonidine is also helpful in some patients with postoperative pain, post-herpetic neuralgia, and other types of neuropathic pain.

Cannabinoids. Data on the efficacy of cannabinoids for cancer patients with neuropathic pain are limited, but cannabinoids are recommended for refractory pain in patients with multiple sclerosis or peripheral neuropathy (Attal et al. 2010). In two randomized controlled studies, smoked cannabis relieved the pain of HIV neuropathy (Abrams et al. 2007; Ellis et al. 2009).

Cannabinoids have been shown in several placebo-controlled trials to be as effective as codeine (Johnson et al. 2010). The cannabinoid extract tetrahydrocannabinol:cannabidiol (THC:CBD) spray was an effective adjuvant in decreasing pain compared with placebo or THC spray in patients with advanced cancer and moderate to severe levels of cancer pain on chronic opioid therapy. The spray containing THC alone was not effective (Johnson et al. 2010).

Ketamine. Ketamine is a pure NMDA antagonist that is typically used as an anesthetic but can be helpful for selected patients with neuropathic pain

that is resistant to the combinations of agents discussed above. Ketamine is particularly helpful for patients with central sensitization who cannot get pain relief without sedation and who wish to be awake. Patients who are taking ketamine describe being "dissociated" from their pain. They know it's there, but it's not theirs. Unfortunately, they can also be more generally dissociated, and for some this can be frightening, as can the strange dreams and even daytime hallucinations that sometimes occur. Benzodiazepines (e.g., lorazepam 1 mg), rather than neuroleptics, are effective in reversing these side effects (Mercadante et al. 2000).

Two randomized controlled trials, methodologically sound, found that ketamine (intrathecal [Yang et al. 1996] or IV [Mercadante et al. 2000]) allowed a reduction in the use of morphine and produced a significant improvement in pain control for patients with neuropathic cancer pain (Bell et al. 2003). Ketamine is particularly useful as a bridging agent, to provide pain relief for a few days when rotating a patient to methadone, or treating a patient with opioid neurotoxicity (Moryl et al. 2009).

PRACTICE POINTS: KETAMINE FOR REFRACTORY PAIN

- Inform the patient that he is likely to experience a "dreamlike" state.
- Give a ketamine bolus of 0.1 to 0.2 mg/kg IV or 0.5 mg/kg SQ, monitoring vital signs.
- If there is no change in the pain, double the dose of ketamine at 15 minutes (for IV dosing) or 45 minutes (for SQ dosing).
- Repeat step 3 [doubling of dose] until pain relief is achieved, and then begin a continuous IV or SQ drip to deliver the equivalent amount. For example, a patient who required a total of 12 mg of ketamine in 60 minutes should be started on a drip of 12 mg/hr. Increase the drip as needed and tolerated.
- If a decrease in opioid dose is desirable because of opioid side effects (e.g., myoclonic jerks), decrease the opioid dose initially by 50 percent when the ketamine drip is begun, and halve again every 24 hours as tolerated.
- Excess salivation may require additional therapy such as scopolamine (Transderm Scōp), hyoscyamine (e.g., Levsin), or glycopyrrolate.

(From Fine 2003)

Ketamine administration has been successfully converted to the oral route, but dosing is affected by the drug's active metabolite, norketamine. Levels of norketamine are two to three times higher with oral dosing of ketamine than

when given parenterally, so the oral ketamine dose is about one-third the parenteral dose (Fitzgibbon et al. 2002).

Intravenous lidocaine infusion. Intravenous lidocaine is a rarely used but effective neuropathic pain adjuvant. Case reports of patients with post-herpetic neuralgia suggest giving doses of 5 mg/kg intravenously over 30 minutes (Rowbotham et al. 1991). Ferrini (2000) reported on the experience of the San Diego Hospice Corporation with prolonged lidocaine infusions for hospice patients with intractable pain. The infusion was initiated in the inpatient hospice unit, titrated down to the lowest effective dose, and then continued in the patients' homes.

The protocol called for starting with a 1 to 3 mg/kg intravenous loading bolus of lidocaine over 20 to 30 minutes (with careful supervision by a physician, registered nurse, or nurse practitioner), recording of vital signs every 15 minutes, and assessment of pain and side effects. If the bolus was effective, the infusion of an 8mg/ml lidocaine solution was begun at a rate of 0.5 to 2 mg/kg/hr, with a range of 10 to 80 mg/hr. Ferrini urges caution in using lidocaine for patients with severe hepatic insufficiency or heart failure, but low doses may be tolerable and effective. You can give the lidocaine subcutaneously, but prolonged subcutaneous infusions may result in erythema and induration of the infusion site.

In Ferrini's study, lidocaine serum levels were tested in the first 24 to 72 hours and were not drawn again unless there were dose escalations or toxic side effects. Adverse effects such as lightheadedness, perioral numbness, a metallic taste in the mouth, tinnitus, and blurry vision occurred within the therapeutic range of lidocaine, which is a serum range of 2 to 6 μg/ml. When this range is exceeded, patients can develop hallucinations, dissociation, myoclonus, and hypotension (at approx. 8 μg/ml). Stop the infusion immediately if any of these occur, monitor the airway, and for the psychiatric side effects, consider adding a benzodiazepine or a fast-acting barbiturate if benzodiazepines are contraindicated. With higher blood levels of lidocaine, seizures, coma, and respiratory or cardiac arrest may occur.

Adjuvant Treatments for Bone Pain

NSAIDs, corticosteroids (see Tables 6.1 and 6.10), bisphosphonates, and receptor activator of nuclear factor κβ ligand (RANK-L) inhibitors (Fornier 2010; Van Poznak et al. 2011; von Moos and Skacel 2012) can serve as pharmacologic adjuvants to opioids for patients with bone pain (Table 6.11). Vertebroplasty/kyphoplasty can relieve the pain associated with vertebral compression fractures.

Radiofrequency ablation is a new technique to relieve metastatic bone pain. External beam radiation is the longest-lasting palliative treatment for bone pain, and radiopharmaceuticals (e.g., strontium chloride 89, samarium-153, rhenium-186 HEDP, and radium-223 chloride [Alpharadin]) (Paes et al. 2011) enhance its effectiveness and are also effective used alone.

Bisphosphonates. These drugs inhibit osteoclast activity and can provide immediate relief of pain due to bony metastases or bone lesions of multiple myeloma. ASCO recommends using either pamidronate (Aredia) (60 to 90 mg IV over no less than 2 hours), or zoledronic acid (Zometa) (4 mg IV over 15 minutes) (Van Poznak et al. 2011). Both have been shown to decrease pain or the need for pain-relieving medications. If the pain returns, repeat doses 3 to 4 weeks apart are often effective. Both drugs have the added benefit of slowing the growth of some tumor metastases and, when given monthly, of preventing fractures from lytic bone metastases in patients with myeloma and breast cancer (Cleeland et al. 2013).

Both cause similar adverse effects. Both can cause an acute phase reaction, which includes a pain flare, fever, and aches in the joints. This acute phase reaction and renal toxicity are more frequent with zoledronic acid. Renal function should be monitored in patients who have baseline impairment or are at high risk for dehydration. Both can cause hypocalcemia in vitamin D–deficient patients and an increased risk of subtrochanteric hip fracture and of osteonecrosis of the jaw (Fornier 2010).

RANK-L inhibitors. Denosumab is a monoclonal antibody that, by inhibiting the ability of the RANK ligand (produced by osteoblasts) to bind to RANK on the surface of osteoclasts and osteoclast precursors, prevents osteoclast maturation, activation, and bone resorption. Denosumab (given as 120 mg subcutaneously every 4 weeks) therefore prevents skeletal-related complications and hypercalcemia as well as lessening bone pain in patients with breast cancer metastatic to bone. In fact, it can cause a hypocalcemia more profound than that caused by the bisphosphonates.

Denosumab causes an acute phase reaction less often than zoledronic acid and does not impair renal function. Denosumab was compared with zoledronic acid in a large randomized study of patients with metastatic bone disease from breast cancer (Cleeland et al. 2013). Fewer patients receiving denosumab had "meaningful worsening" of their pain (defined by the authors as a greater than 2 point increase from baseline). Denosumab delayed by almost 4 months the worsening of pain from no / mild pain to moderate/severe in those whose pain did worsen, and fewer patients on denosumab had increased pain.

Vertebroplasty/kyphoplasty. Pain from benign or malignant compression fractures can be very difficult to treat, especially in older patients who develop confusion and marked worsening of constipation while using the opioid doses they need, even when they are taking NSAID adjuvants. For selected patients (those with very localized intense pain from a new or progressing fracture) (Papaioannou et al. 2002; Tancioni et al. 2011), vertebroplasty or kyphoplasty may be the answer. In both procedures, bone "cement" (polymethylmethacrylate + antibiotics + an opacification agent) is injected under fluoroscopic guidance into the collapsed vertebra to stabilize it; in kyphoplasty, the endplates of the vertebral body are elevated by inflatable bone tamps before the cement is injected. Both procedures can be done in the outpatient setting by an interventional radiologist, a neurosurgeon, or an orthopedic surgeon.

Case reports suggest that these procedures are successful in relieving pain for 70 to 100 percent of patients with compression from osteoporosis (Watts et al. 2001) or malignancy (Jensen and Kallmes 2002; Tancioni et al. 2011), producing short-term documented improvement in pain and disability, mental function, and quality of life (Zoarski et al. 2002) and long-term (1 to 1.5 years) improvement in pain (Jensen and Kallmes 2002; Zoarski et al. 2002). Patients with malignancies are most often also treated with radiation, so it is difficult to assess the long-term contribution of the vertebroplasty, but case reports indicate pain relief within 48 hours that is most likely due to the procedure (Jensen and Kallmes 2002).

The mechanism of the relief is not clear, although some authors have postulated that the injection of the cement causes destruction of nerve endings in the local tissue or necrosis of the tumor (Jensen and Kallmes 2002). Extravasation of the cement, however, causes marked increase in pain that can last for days, as well as damage to the spinal cord or nerve roots from heat or pressure.

Radiofrequency ablation. Radiofrequency ablation (inducing coagulation necrosis by heating tissues to approx. 100°C) has been used to ablate focal tumors. This technique is now being used to treat painful focal tumors in bone, skin, or viscera (Goetz et al. 2004; Patti et al. 2002; Rosenthal and Callstrom 2012).

External beam radiation and radiopharmaceuticals. External beam radiation is an important palliative tool for treating localized bone metastases (Janjan et al. 2009). It provides pain relief for 50 percent of patients within 2 weeks after completing radiation and for more than 75 percent of patients within 2 additional (4 total) weeks, and the relief usually lasts about three months. Palliative radiation given in a single large fraction is optimal for patients whose survival is expected to be 6 months or less. A single fraction produces pain relief just as fast

and for just as long as the more conventional treatments involving ten fractions (Janjan et al. 2009). Longer fractionation schedules are recommended for patients with better prognoses (e.g., patients with metastatic breast cancer), because tumor recurrence requiring repeat radiation is more common after single fraction, and because the bones heal better after multiple fractions.

Systemic radiopharmaceuticals, such as the alpha emitter radium-223 chloride (Alpharadin) (Cheetham and Petrylak 2012), and the beta emitters strontium chloride 89, samarium-153 lexidronam, and rhenium-186 HEDP (approved only in Europe as of 2010) (Paes and Serafini 2010; Paes et al. 2011), are used for patients with diffuse bony metastases.

The newest agent, radium-223 chloride (Alpharadin), utilizes an alpha particle bound to a calcium analogue that self-targets to bone metastases. It is likely to cause less marrow toxicity than the beta emitters discussed below because the range of the alpha particles is only a 2- to 10-cell diameter. Alpha particles can therefore destroy the metastasis with relative sparing of normal marrow cells. The first randomized controlled multicenter phase III trial (vs. placebo) showed a small improvement in survival (OS 14.0 vs. 11.2 months, 2-sided p value = .0022), and phase II studies indicate improved bone pain. Ongoing trials will inform us more about the true utility and comparative toxicity of this alpha-emitting agent for control of the pain of bony metastases.

The beta-particle emitters localize in osteoblastic metastases. They provide pain relief in about 60 to 80 percent of patients (Janjan et al. 2009). Pain relief usually begins within 2 to 4 weeks and is maintained for more than 6 months in patients with breast or prostate cancer. Strontium chloride 89 can prolong the pain relief induced by external beam radiotherapy (Janjan 2001; Porter et al. 1993).

Strontium-89 is chemically similar to calcium and is deposited in bone preferentially to calcium. It may therefore exacerbate hypercalcemia and should not be given to hypercalcemic patients. Strontium chloride 89 is given by slow intravenous push in the outpatient setting by a nuclear medicine physician. For 48 hours after the injection, patients should flush twice after using a toilet and should avoid using urinals and bedpans if possible. Families should be cautioned to wear disposable gloves while handling any items contaminated with the patient's urine, feces, or blood. Patients and families should also be warned that 5 to 10 percent of patients will suffer a "flare" (i.e., an increase in bone pain) 2 to 3 days after the injection, which will remit in 7 to 10 days; flares occur more often in patients with breast cancer than in those with prostate cancer. Corticosteroids or NSAIDs may relieve the pain.

Pregnancy and breastfeeding are the only two absolute contraindications to use of strontium-89, and patients should be cautioned not to get pregnant for

6 to 12 months after the injection. Patients with GFR less than 30 ml/min should not be treated because of the risk of prolonged myelosuppression, but those with clearances between 30 and 50 ml/min can be given a 50 percent dose reduction.

Myelosuppression occurs in most patients. The nadirs occur at 4 to 8 weeks, and counts are somewhat recovered by 12 weeks. Initial blood counts and previous irradiation of marrow do not predict the extent of the subsequent reductions in blood counts. Platelet and leukocyte counts usually fall 25 to 40 percent. Strontium chloride 89 is therefore contraindicated for patients with hemoglobin less than 9 mg/dL, platelet counts of less than 100,000/mm^3, or absolute leukocyte counts of less than 3500/mm^3 (Paes and Serafini 2010). Life-threatening thrombocytopenia, however, has been noted in patients with low-grade disseminated intravascular coagulation (DIC) or rapidly falling platelet counts, and some researchers suggest obtaining DIC screens for such patients prior to strontium chloride 89 therapy. If DIC is excluded, patients with lower values of at least 60,000 platelets/mm^3 or 2400 WBC/mm^3 may be treated safely.

Pain relief is more rapid with samarium-153 lexidronam and rhenium-186 than with strontium. Seventy percent of patients have pain relief, and it occurs within 1 to 2 weeks. Patients should be monitored for opioid toxicity, therefore, and doses lowered as needed. Hematologic recovery is also more rapid and is usually complete within 8 weeks. Since samarium-153 lexidronam and rhenium-186 are excreted intact in the urine, patients and families should exercise the same precautions as they would if the patient had received strontium, but the excretion is complete within 12 hours. The same contraindications to therapy described for strontium apply to samarium-153 and rhenium-186.

Hemibody radiation is as effective as strontium chloride 89 for patients with prostate cancer but is more toxic (Janjan 1997). Hemibody radiation can relieve pain in the lower spine, pelvis, and femora in as many as 80 percent of prostate cancer patients, with 30 percent obtaining complete relief. The relief begins as early as 48 hours after treatment but lasts a median of only 15 weeks. A randomized study indicated that patients treated with fractionated rather than single-dose regimens experienced longer durations of response (8.5 vs. 3 months) and a decreased need for retreatment (13 percent vs. 70 percent). Hemibody radiation, however, is not often chosen as the initial therapy for patients with bony metastases because of technical difficulties in delivering the radiation, side effects of the therapy, and concerns about toxicity to viscera and bone marrow in the treatment field.

PRACTICE POINTS: TREATING PATIENTS WITH BONE PAIN

- For patients over 60 years old or with congestive heart failure, renal disease, asthma, or a history of gastrointestinal bleeding, the risks of NSAIDs (used as opioid adjuvants for bone pain) probably exceed the benefit.
- Bisphosphonates: Give zoledronic acid (Zometa) or pamidronate for pain due to bone metastases. Both can also decrease pathologic fractures in patients with metastatic breast cancer or multiple myeloma. Use pamidronate for patients with renal insufficiency.
- RANK-L inhibitors: RANK-L inhibitors (e.g., Denosumab) are effective for pain from bone metastases but can cause severe hypocalcemia in patients with deficiencies of vitamin D. Such patients will require repletion of both vitamin D and calcium.
- Vertebroplasty and kyphoplasty can relieve the pain associated with vertebral compression fractures caused by either osteoporosis or cancer.
- Radiofrequency ablation and external beam radiation are designed for patients with few painful bony metastases. For patients with refractory diffuse bone pain, consider referring the patient to a nuclear medicine specialist for a systemic radiopharmaceutical: either a beta-emitter (e.g., samarium-153 lexidronam) or an alpha emitter (e.g., Alpharadin).

Neuroleptics

Neuroleptic agents include the butyrophenones, such as haloperidol (e.g., Haldol), and the phenothiazines, such as chlorpromazine (e.g., Thorazine). In cancer patients, these agents are most useful in treating patients with delirium, though chlorpromazine can also help those with dyspnea or intractable hiccups. Although most butyrophenones and phenothiazines are not useful in relieving pain, there is some evidence that the butyrophenone pimozide, which is used for patients with Tourette's syndrome and resistant tics, has analgesic activity. Pimozide may be useful for patients with pain syndromes that resemble trigeminal neuralgia, but results of studies are conflicting.

Skeletal Muscle Relaxants

Skeletal muscle relaxants include agents such as baclofen, diazepam, tizanidine, and dantrolene, which are used for spasticity, and carisoprodol (e.g.,

Soma), metaxolone (Skelaxin), chlorzoxazone (e.g., Parafon Forte DSC), cyclobenzaprine HCl (e.g., Flexeril), methocarbamol (e.g., Robaxin), and orphenadrine citrate (e.g., Norflex, Norgesic), which are skeletal muscle relaxants (Chou et al. 2004). Only baclofen is FDA approved for spasticity. Used alone, they are no more effective than NSAIDs, but they do add to the efficacy of NSAIDs for patients with acute muscle injury and spasm. Carisoprodol, orphenadrine, and methocarbamol are available in preparations that include aspirin.

Skeletal muscle relaxants are not as effective for patients with chronic nonmalignant pain as for those with acute pain, and they have not been studied in patients with cancer pain. Because they are metabolized by the liver and excreted by the kidneys, skeletal muscle relaxants are relatively contraindicated for patients with renal or hepatic dysfunction. In addition, they have the potential for abuse, and patients who stop them suddenly may experience a withdrawal syndrome.

Muscle relaxants cause significant side effects. Drowsiness is especially problematic and is likely to limit their use in someone receiving other sedating agents such as opioids. They can also cause dizziness, headaches, blurry vision, agitation, confusion, hallucinations, and convulsions. More rarely, patients have developed abdominal pain, nausea, vomiting, or anorexia when taking these drugs. Cyclobenzaprine HCl is related chemically to tricyclic antidepressants, and orphenadrine citrate is related to diphenhydramine; they share the anticholinergic and antihistaminic side effects of these agents.

For cancer patients who develop an acute muscle injury or muscle spasm and who do not need opioid analgesics, a combination NSAID / skeletal muscle relaxant may be beneficial. Because of the serious side effects they can induce, do not prescribe them for prolonged periods.

A *benzodiazepine* such as diazepam (e.g., Valium), which is FDA approved for spasticity, can help cancer patients who have muscle spasms, even those induced by spinal cord injury, but it is no more effective than the other skeletal muscle relaxants or baclofen. The side effects of this long-acting agent limit its usefulness, especially for patients who require concomitant opioid therapy. Patients who have been using diazepam chronically for an anxiety or seizure disorder are likely to tolerate the combination of an opioid and the diazepam. Other patients are likely to develop intolerable somnolence.

Smooth Muscle Relaxants

Pain arising from the smooth muscle of the gastrointestinal tract is due to either stretching, as is experienced during a bowel obstruction, or intense contractions.

Contractions can cause cramping, and if the contraction moves through an area of injured mucosa, such as would occur in esophagitis or in radiation injury to the rectal area, the pain can be intense. Such pain is intermittent and often difficult to control with basal opioids, because a basal dose adequate to control the pain at its height causes unacceptable sedation between painful episodes. Patients receiving opioids for another cause of pain, who are opioid tolerant, however, may get significant immediate pain relief from any of the various forms of transmucosal fentanyl (oral tablet, film, or nasal spray). The onset of pain relief in about 5 minutes and the disappearance of opioid effect in about an hour make this form of opioid delivery particularly helpful for these patients.

Another approach is to relax the smooth muscle (Table 6.12). Calcium channel blockers like nifedipine, gabapentin, or pregabalin can be helpful as can baclofen. In patients with adequate blood pressure, nitroglycerin can relieve esophageal spasm. Anticholinergic agents also relax gut smooth muscle. Dicyclomine (e.g., Bentyl) (10–20 mg p.o. up to t.i.d. p.r.n.) has minimal other anticholinergic side effects and is often effective.

Local therapies are also effective. Belladonna and opium suppositories (B&O Suppositories) provide significant relief for patients with bladder or rectal spasm. Patients can use 30 or 60 mg up to four times a day. For those with rectal spasm, it may be necessary to pretreat the rectal area with a lidocaine or hydrocortisone cream (e.g., Anusol) to enable the patient to tolerate insertion of the suppository. Refer refractory patients with rectal pain to an anesthesia pain specialist for consideration of a block of the ganglion impar (discussed later in this chapter).

Anesthetic Methods of Pain Relief

Anesthetics and anesthetic pain techniques play a select but valuable role in relieving pain for certain cancer patients. They are most helpful in the fewer than 10 percent of patients with significant neuropathic pain that has not been relieved by any of the techniques discussed thus far. Anesthetics are available in topical and oral formulations as well as the parenteral forms that are needed to numb or ablate peripheral or spinal somatic or autonomic nerves, or to block transmissions from the spinal cord.

The parenteral anesthetic agents are indicated for patients with significant neuropathic cancer pain that has not been satisfactorily relieved by combinations of oral or transdermal opioids, adjuvant agents, and topical or oral anesthetics. They are delivered by anesthesia pain specialists who practice both in free-standing and in hospital-based pain clinics. These physicians are often

leaders of multidisciplinary teams involved in research, education, and clinical care of patients with neuropathic pain. Very few cancer patients will ever need to be referred to an anesthesia pain specialist, but for those who do, the quality of their remaining life can be greatly improved.

In what follows, I provide an overview of the techniques they use and a description of the types of patients they can help. As I am not an anesthesia pain specialist, I do not feel qualified to describe the techniques themselves in detail, but references are provided at the end of the chapter.

Topical Anesthetics and Parenteral Lidocaine

Topical anesthetics are of limited general utility in cancer patients with pain, but they can be helpful in selected instances. The preparations available include a combination of lidocaine and prilocaine (EMLA), lidocaine alone (e.g., ELA-Max), and capsaicin (Table 6.13).

EMLA. This cream includes a mixture of two anesthetics, lidocaine 2.5 percent and prilocaine 2.5 percent. It anesthetizes the skin to a depth of about one-quarter inch (5 mm) and is used, for example, before accessing a subcutaneous port, placing a peripherally inserted central catheter (a PICC line), or doing a lumbar puncture, bone marrow aspiration, or biopsy. The majority of studies have taken place in children, but adults may also benefit from its use.

An hour to 90 minutes before the planned procedure, the nurse, the patient, or a family member places a mound of EMLA cream over the area to be anesthetized, using about half of a 5-g tube. Being careful to maintain a thick layer of cream, the person applying it covers the mound with a semipermeable dressing such as Opsite or Tegaderm. Immediately before the procedure, the dressing and cream are removed and the area is prepared as usual. The skin anesthesia will remain for up to 4 hours.

Side effects of EMLA are minimal. The prilocaine in the anesthetic mixture can cause increases in methemoglobin, but when EMLA is used as recommended, methemoglobinemia has not been a problem, even in children as young as 3 months old. The only other consistent findings are changes of skin color to red or white; this rarely lasts longer than 4 hours.

Lidocaine gel, ointment, or patch. Topical lidocaine gel (5 percent) was shown to be more effective than placebo in relieving pain in a double-blind controlled trial in patients with post-herpetic neuralgia (Rowbotham et al. 1995). Lidocaine ointment (5 percent and 10 percent) is also available and can be used along with capsaicin for post-herpetic neuralgia or alone for peripheral sensory

neuropathy. ELA-Max, a cream containing 4 percent lidocaine, is now available over-the-counter as an alternative to EMLA cream. Because it does not contain prilocaine, there is no risk of methemoglobinemia.

Lidocaine patches (e.g., Lidoderm) are lidocaine-impregnated dressings that adhere to the skin and deliver anesthesia to the skin surface. The patch is FDA approved for use in post-herpetic neuralgia and has been reported to be effective in patients with other chronic neuropathic pain syndromes, such as diabetic neuropathy and post-mastectomy and post-thoracotomy pain.

Lidocaine patches can be placed on skin that is so hyperesthetic that even the touch of clothing is uncomfortable. Hyperesthesia can occur in patients with post-herpetic neuralgia or in those with nerve injury from surgery (e.g., post-thoracotomy or post-mastectomy) or from tumor invasion of either peripheral nerves or dorsal root ganglia. The patches should be applied to intact skin for up to 24 consecutive hours a day, and can be cut to size. As many as four patches can be used concurrently. Systemic concentrations of lidocaine do not reach a level at which they would affect cardiac function. Lidocaine patches should not be used where the skin is broken or over skin directly in the radiation port when the patient is receiving radiation therapy.

Capsaicin. Capsaicin cream (0.025 percent, 0.075 percent) (e.g., Zostrix, Capzacin-P) has been approved by the FDA for arthritis pain, for postsurgical neuropathic pain, and for treatment of post-herpetic neuralgia, where it can be used along with gabapentin or pregabalin. It is also a useful addition to NSAIDs for patients with pain from bony metastases.

Capsaicin provides analgesia by depleting substance P, a peptide that is an important transmitter of nerve impulses from peripheral nerves to the spinal cord. Capsaicin is found in the seeds of hot peppers and is what causes the intense burning and numbness you've experienced if you've made the mistake of eating one.

Unfortunately, capsaicin cream is expensive, and it usually provides only partial pain relief, being effective in about half the patients with post-mastectomy and other postsurgical neuropathic pains who were surveyed, and in up to one-third of patients with post-herpetic neuralgia. Repeated applications (four times a day) for at least 4 weeks are needed. Adhesive skin patches delivering 0.025% capsaicin can be used but have not been tested for this indication.

Further, capsaicin's utility in relieving neuropathic pain is limited by the significant burning it causes in the skin where it is applied. Patients with post-herpetic neuralgia experience more discomfort using the cream than those with post-mastectomy pain, but it occurs in both populations and was the most common reason patients stopped using capsaicin. Some patients have found that

applying a 5 percent or 10 percent lidocaine ointment prior to the capsaicin cream diminished the burning sensation; others, even with the lidocaine pretreatment, could not tolerate this agent (Watson et al. 1988).

Capsaicin may cause intense burning in these patients because their nerves are injured and their skin is hyperesthetic. Patients with normal skin who use capsaicin cream for arthritis or deep muscle pain notice warmth, but they tolerate it very well. They rub it into the skin over the painful area once to three times a day. The area sometimes becomes warm if it is exposed to water or to sun, but not painfully so.

Local Anesthetics Taken Orally

Mexiletine, a local anesthetic available in pill form, is an effective adjuvant for certain patients with refractory continuous or lancinating neuropathic pains (Table 6.13). It is usually reserved for patients with refractory neuropathic pain that has not responded to the agents discussed above.

Mexiletine use for patients with neuropathic cancer pain has not been studied extensively, but it is the most often used oral local anesthetic for patients with nonmalignant neuropathic pain. It is relatively safe even for patients with a cardiac arrhythmia or those receiving drugs to prevent one. The initial recommended dose is 150 mg/day orally, and it can be escalated if tolerated to doses of 300 mg orally three times a day. Dyspepsia and diarrhea may limit its tolerability.

Neural Blockade and Neuroablation

Neural blockade and neuroablation are the province of interventional radiologists and anesthesia pain specialists. These techniques are often employed as initial therapy for post-thoracotomy syndrome, acute pain from herpes zoster (neural blockade alone), post-herpetic neuralgia, or pain from pancreatic cancer, but they are otherwise used only when the therapies mentioned elsewhere in this chapter have been ineffective.

The only patients with refractory neuropathic pain who are unlikely to benefit from neuroablative procedures are those with *deafferentation* pain. Deafferentation pain is a poorly localized, deeply aching, and distressing sensation that occurs when a peripheral nerve is "disconnected" from the spinal cord surgically or by any other process that injures a nerve. Patients with injury to the spinal cord from cancer or with tumor invading the brachial or lumbosacral plexus can develop deafferentation pain. Though such patients might experience

temporary relief from a local anesthetic block, a neurolytic procedure is unlikely to be of benefit.

Neural blockade. Neural blockade is a regional anesthetic procedure that can include blocks of spinal and peripheral somatic nerves and of the sympathetic nervous system. Injections of local anesthetics such as lidocaine or bupivacaine along with a corticosteroid are used for diagnosis, prognosis, therapy, and pain prevention.

A *diagnostic* nerve block can determine which nerve is mediating the pain and whether it is a somatic or sympathetic nerve. The anesthesia pain specialist can then plan the appropriate therapeutic block or neurolytic procedure. The patient's response to this block will also allow the specialist to predict the likely outcome and the side effects of a more permanent procedure (e.g., neuroablation).

To minimize ineffective procedures, the American Society of Anesthesiologists' Task Force on Pain Management, Cancer Pain Section (Ferrante et al. 1996), recommends that *prognostic* blocks always precede a planned neuroablative procedure; if anesthetizing the nerve does not relieve the pain, the anesthesiologist does not proceed. Unfortunately, the converse is not true: a positive result from a block does not always predict a positive outcome from the neuroablative procedure.

Sometimes, *therapeutic* nerve blocks are sufficient, and a neuroablative procedure will not be needed. Interestingly, their effectiveness may outlast the known half-life of the anesthetic agent that was injected. Anesthetics, in combination with a glucocorticoid, can be injected into the spinal space or nerve roots affected by tumor, and the relief can last from days to weeks. *Trigger point injections* can help with myofascial pains, such as those associated with post-mastectomy syndrome. A local anesthetic is usually injected into the trigger point, though dry needling or local instillation of saline or corticosteroid are also used. Before adding systemic opioids to NSAIDs for patients with myofascial pain, refer them for trigger point injections.

Subcutaneous administration of local anesthetic plus corticosteroids is often helpful for the somatically mediated acute pain of herpes zoster and for prevention of post-herpetic neuralgia. Because these injections are so often effective and have so few associated side effects, consider referring patients with these syndromes to an anesthesia pain specialist before beginning therapy with opioids or an adjuvant such as gabapentin or pregabalin.

Radiofrequency ablation. Radiofrequency ablation (inducing coagulation necrosis by heating tissues to approx. 100°C) has been used to treat patients with trigeminal neuralgia (tic douloureux) by destroying the trigeminal nerve ganglion.

Sympathetic nerve blocks of the celiac plexus or the stellate or gasserian ganglia are usually done as diagnostic and prognostic procedures in patients with pancreatic cancer or with cancer of the head and neck, respectively. A chemical neurolytic procedure or radiofrequency lesioning is performed if anesthetic blockade of the relevant sympathetic structure results in remission of the pain.

Sympathetic nerve blocks are also often used for patients suffering from Type I complex regional pain syndrome (formerly termed *reflex sympathetic dystrophy*, or *causalgia*), which arises from injury to sympathetic nerves due to trauma, scarring, or direct invasion by a malignancy. The patient complains of burning pain in the arm or leg, and the limb becomes hyperalgesic and allodynic (i.e., even clothing touching the skin causes a burning pain). The skin may be edematous, red or pale, may manifest decreased sweating and increased warmth, and, over time, will become atrophic. You may note such changes in the arms of patients with infiltration of the brachial plexus due to cancers of the breast or superior sulcus of the lung, or those who have received radiation to the brachial plexus. In some cases the pain syndrome will respond to a blockade alone, but in others, chemical destruction of involved ganglia or surgical rhizotomy (i.e., selective ablation of the affected ganglia) is needed.

Neurolytic procedures. Neurolytic procedures (i.e., ablation of the nerve) are indicated for patients who are expected to live only a short time, whose neuropathic pain is well localized, and whose pain has not responded to other measures. Pain mediated by spinal, peripheral somatic, and sympathetic nerves can be treated by these techniques.

Neuroablation can be achieved surgically, but at present, thermal and chemical means are more commonly used. Thermal techniques include radiofrequency ablation, as discussed above, and cryoanalgesia. Chemical agents include glycerol (which is used to block the trigeminal ganglion), phenol, and ethanol. Phenol, unlike ethanol, has local anesthetic as well as lytic effects and is therefore painless when injected. Ethanol injections are so painful that they must be preceded by injections of local anesthetic, and the patient must be sedated. The usual clinical doses of phenol or ethanol are unlikely to cause side effects from systemic absorption. If phenol is injected intravascularly by accident, however, it can cause convulsions, CNS depression, and cardiovascular collapse.

Spinal Neurolytic Procedures. Patients suffering from recurrent gynecologic, colorectal, or bladder cancers may experience severe bilateral pelvic pain in a "saddle" distribution. Systemic opioids or a spinal opioid/anesthetic infusion usually provides these patients with satisfactory pain relief. For over 60 percent of the very few who still have intolerable pain, subarachnoid neurolytic blockades may provide good pain relief for several months; rarely, pain relief

lasts up to a year. The pain relief may be so complete that the patient abruptly discontinues all oral opioid therapy. To prevent patients from experiencing withdrawal, they are instructed before the procedure on how to taper their opioids safely.

Saddle blocks are considered when a spinal catheter cannot be used or its insertion is problematic, as can be the case for patients with frequent infections, lack of home care coverage, or a family situation too unstable to assure safety of the epidural catheter. Patients with, for example, a rectovaginal fistula or burning perineal pain from locally advanced pelvic cancers (e.g., colorectal, bladder, cervical, or endometrial cancer) may benefit from these blocks. Phenol, which is hyperbaric, is placed intrathecally and sinks to the level of S2–S4 nerves. Patients usually continue to be mobile, but the block may cause bowel and bladder incontinence. Usually, however, patients who need this block for pain relief already have diverting colostomies, ureters diverted into Indiana pouches, or renal stents to relieve obstruction caused by the tumor. Side effects (e.g., leg weakness) and pain relief depend on the concentration of phenol used. Higher concentrations of phenol can be given to patients with urinary diversions. Generally, patients have at least a 50 percent pain reduction and clearer thinking, because systemic agents can be markedly reduced. Relief usually lasts for a month, but it sometimes lasts for two months and, rarely, can persist for as long as six months.

Subdural and epidural neurolysis is used for pain in the cervical region, an area in which subarachnoid blockade is not effective. It can be helpful to patients with refractory pain due to cancer of the ear, nose, throat, or lung, or for those with bony cervical metastases.

Ablation of Peripheral Somatic Nerves. *Neuroablation of intercostal nerves* can relieve post-thoracotomy syndrome, especially when performed within six months of its onset. This procedure can also relieve the pain of a pathologic rib fracture in someone who is not a candidate for radiation therapy. Neuroablation is also used for patients with intractable pain from metastatic lesions to tissues innervated by other peripheral nerves, such as a metastatic tumor to the forearm, which is innervated by the superficial radial, lateral cutaneous, and posterior cutaneous nerves (Turnbull et al. 2011). Because neuroablation is often so effective and has so few associated side effects compared with the doses of systemic opioids or neuropathic adjuvant agents that would be needed, consult with an anesthesia pain specialist as soon as possible.

Sympathetic Nerve Ablation. Some patients' neuropathic pain syndromes are caused by injury to the sympathetic nervous system. The injury can be to ganglia or to the sympathetic fibers in a nerve plexus such as the brachial or lumbosacral plexus.

PERIPHERAL NEUROABLATIVE PROCEDURES

Target	*Indications*
• Sacral nerves	Perineal pain
• Intercostal nerve	Post-thoracotomy syndrome
• Sympathetic ganglia:	
—Celiac plexus	Upper abdominal pain
—Inferior mesenteric (impar)	Perineal, rectal pain
—Stellate	Head and neck pain
—Gasserian	Tic douloureux–like pain
• Hypogastric plexus	Pelvic pain
• Percutaneous dorsal rhizotomy	Complex regional pain syndrome type I (causalgia) of upper extremity

Head, Neck, and Upper Extremity. In the past, injection of the *gasserian ganglion* with alcohol was used for patients with benign or malignant causes of tic douloureux. More recently, however, for patients with pain refractory to carbamazepine or baclofen, injection of the ganglion with glycerol, thermogangliolysis, or surgical rhizotomy is used.

Sympathetic blockade of the *stellate ganglion* with local anesthetics can reduce the incidence of post-herpetic neuralgia in the upper extremity and face if used within two weeks of the onset of the herpes zoster. Some researchers have found that it can be effective if used within the first two months of appearance of the lesions.

Selected cancer patients with pain in the arms or in the head and neck or with Pancoast tumor will benefit from neuroablation of the stellate ganglion. Chemical neuroablation is rarely done, because of the damage that may be caused to nearby nervous, vascular, and brain structures by the lytic agents.

Some patients with injury to the brachial plexus have complex regional pain syndrome type I (causalgia) that does not respond to anesthetic blockade. For these patients, *percutaneous surgical dorsal rhizotomy* is considered preferable to a chemical rhizotomy because it rarely has to be repeated.

Abdominal/Pelvic. The most commonly used and most effective sympathetic neurolytic blocks for cancer patients have been blocks of the *celiac plexus*. This plexus contains sympathetic ganglia that mediate pain from upper abdominal organs. Celiac plexus blocks have been found to relieve the pain of half to three-quarters of patients with pancreatic cancer. Because the blocks are so effective, some surgeons will resect the celiac ganglion or inject it with alcohol or a phenol

solution at the time of definitive or palliative surgery. Anesthesia pain specialists and interventional radiologists perform the neuroablation percutaneously with fluoroscopy or CT guidance. GI specialists can do it during endoscopy.

A celiac block may also relieve pain due to cancer of the stomach, liver, small bowel, proximal colon, or abdominal metastases if it resembles the pain caused by pancreatic cancer. Celiac blocks do not have to be reserved for patients who are refractory to opioids or for whom the opioid-induced side effects are poorly tolerated. A randomized double-blind controlled trial showed that celiac plexus block done at the time of diagnosis in patients with inoperable pancreatic cancer decreased the need for systemic opioids to control pain throughout the patient's course (Wyse et al. 2011). The effects were particularly evident 3 months after randomization, and strongest in patients who did not have chemo-XRT for their cancer.

The common side effects caused by destroying the celiac plexus result from interruption of the sympathetic innervation to the upper abdominal organs. They include temporary orthostatic hypotension and diarrhea due to increased gut motility. Rarely, the neurolytic solution will spread to the lumbosacral plexus or nerve roots and cause radicular pain or, very rarely, paraparesis or paraplegia.

Chemical neuroablation of the *superior hypogastric plexus* is very effective in the treatment of selected patients with pelvic cancer pain, such as that caused by gynecologic or recurrent colorectal cancer. Relief can last as long as six months. The older procedure, chemical lumbar sympathectomy, has also been shown to be effective for pelvic pain, but the blockade is less selective.

Rectal pain / tenesmus and perineal pain respond to blockade of the *ganglion impar*, located anterior to the sacrococcygeal ligament. Complications include puncture of the rectum and bladder, local infection, and abscess. Spinal anesthesia and intravascular injection may rarely occur.

The anesthetic techniques reviewed above are often crucial to providing effective therapy for the less than 10 percent of patients for whom opioids and adjuvant agents have caused intolerable side effects or have failed to relieve their neuropathic pain. By recognizing neuropathic pain when it occurs, using the topical and oral agents judiciously, and referring appropriate patients to anesthesia pain specialists, you may enable your patients with very refractory pain syndromes to experience significant relief.

Relieving Pain in Older Persons

Assessment

Staff in long-term care facilities, community nurses, and even hospice nurses underestimate intense levels of persistent pain in elderly patients and consequently undertreat them. Dementia is estimated to occur in about 5 percent of patients over 65, rising to more than 40 percent in patients over 85, and cognitively impaired patients pose a particular challenge. (Ideally, you will be able to collaborate with either the geriatrician or the geriatric psychiatrist caring for the patient.) Inadequate supplies of potent opioids, lack of trained staff to perform the assessments, and lack of expertise among physicians responsible for these patients all contribute to inadequate pain management in this setting. Even the pain of cancer patients living in nursing homes is undertreated. Most receive no opioid analgesia or only a step 2 agent for their pain.

It is often difficult to assess the degree of pain that older cancer patients experience. They have pain as frequently as younger patients and are able to describe its location and qualities (sharp, dull, etc.) just as accurately, but older patients less often report their pain. This may be because they ascribe any new pain to a co-morbid condition such as arthritis and don't realize that it may be due to the cancer. Alternatively, they might just be more stoic, expecting to experience more pain as they age and not wanting to distress those around them.

Pain assessment in either the frail older patient or in patients who are cognitively impaired requires some modification of the techniques described in Chapter 5, which includes a copy of the PAINAD scale, a validated tool for assessing pain in this population (Warden et al. 2003). Try to determine how well the patient performs the usual activities of daily living, and gauge the success of the treatment by improvements in functional measures. If you use a pain assessment tool, choose one that the patient finds easy to use, such as a *word scale* (mild, moderate, severe, excruciating), a *pain thermometer,* or a *face scale*. Also, refer to pain behaviors, such as those listed in Table 6.14.

The key to achieving pain control in cognitively impaired patients seems to be frequent assessment. Repeated questioning is needed because, while these patients accurately report the pain they are currently experiencing, they are often unable to recall previous pain intensity. To adjust opioid doses in cognitively impaired patients, assess the intensity of their pain before they received pain medication, then repeat the assessment an hour or two later.

Management Considerations

Once you understand the nature of the pain an older patient is experiencing, there are two other important factors to consider: (1) the role of family members in caring for older patients and (2) the pharmacokinetic and pharmacodynamic differences between the metabolism of pain-relieving drugs in older persons and that in younger persons.

Family members. Family members are often the key to success in managing the pain of older patients. But physicians need to recognize how difficult this may be for caregivers, especially if they are elderly themselves. They spend a great deal of time taking care of the person in pain, often relinquishing their own jobs or accustomed routines in the home. The caregivers are often sleepless and exhausted, and feel inadequate to the task and helpless as they watch the suffering of their loved one. They may fear causing addiction from potent opioids as much as the pain itself. Supporting and educating them is crucial to the well-being of the entire family.

PRACTICE POINTS: PAIN MANAGEMENT IN OLDER PERSONS

- Assure patients and their families that you want to hear about each of the patient's pains.
- Identify a pain scale they understand and can use.
- In cognitively impaired patients, pain *now* is more accurate than remembered pain. Use the PAINAD scale.
- Involve caregivers and home nursing services in monitoring the effectiveness of the regimen and the occurrence of side effects.
- Avoid NSAIDs. If they are used, monitor carefully for side effects and exacerbations of congestive heart failure, cirrhosis, hypertension, or renal insufficiency. Consider gastrointestinal prophylaxis.
- Respect altered pharmacokinetics and pharmacodynamics of drugs in these patients.
  - —Give lower initial doses of benzodiazepines, gabapentin, pregabalin, and opioids. Increase doses slowly.
  - —Give drugs with short half-lives that are the least sedating and have the fewest anticholinergic side effects.
- Institute aggressive regimens to prevent constipation.

Home nursing and home hospice services are invaluable in helping ease the family's physical and psychological burdens. The nurses provide expert evaluation and management of the patient's symptoms, along with patient and family education and guidelines on when to contact the physician. The social workers and chaplains can address the psychosocial and spiritual needs of both the patient and the caregiver. And home health aides and volunteers can give the older caregiver a much-needed break—either by doing some of the patient care or by sitting with the patient so that the spouse can rest or take a walk.

The Burden of Caregiving

The burden of the caregiver's responsibility was brought home to me by Mr. O'Hara, a 79-year-old man with metastatic bladder cancer and complete ureteral obstruction that required bilateral stents. He lived with an older sister who was dying of multiple noncancerous medical problems. Because of his own physical deterioration, Mr. O'Hara had agreed to receive home hospice services from the same visiting nurse agency that was helping his sister. They received health aide services for as much as 8 hours a day, but for the remaining 16 hours, Mr. O'Hara was the sole caregiver for his sister. And he maintained that role until her death.

After she died, he moved into a community home for older people. About a month later, the hospice coordinator got in touch with me. It seemed that Mr. O'Hara was doing so well that they wanted to discontinue the hospice services! What we had attributed to progressive cancer was actually the exhaustion and debilitation caused by caring for his dying sister. One month after her death, he had gained weight, had less pain, and seemed to need no services from the hospice staff. He did well for at least two more years, after which I lost touch.

As there was no one else to help him, and his financial resources were limited, we were unable to provide all the support Mr. O'Hara needed. But even when other people are willing to pitch in, family caregivers are often reluctant to let them. One of your major challenges, in fact, may be to convince the spouse or other person primarily caring for the patient to let others help as much as possible—to involve willing family and friends and accept community services. Primary caregivers need to accept that their own health may be endangered if they shoulder the burden alone and that, if they fall ill, there will be no one left to care for the patient at home. Accepting help may be the only solution.

Pharmacokinetic and pharmacodynamic alterations in older persons. Both the pharmacokinetics (the absorption, metabolism, and excretion of the drug)

and pharmacodynamics (the effects of the drug at various serum levels) of NSAIDs, adjuvants, and opioids are different in older patients. Older persons have less muscle and more fat than younger persons, and their renal and hepatic functions are often mildly to moderately impaired, leading to less rapid hepatic and renal drug clearance. Older patients often suffer from concomitant medical illnesses, and they are more sensitive to opioid-induced sedation and confusion.

NSAIDs can be particularly problematic in the older patient. Of the choices available for mild to moderate pain, acetaminophen (<3 g per day) is the agent recommended by the American Geriatrics Society (American Geriatrics Society Panel 2009; Gloth 2011). Naproxen or low-dose ibuprofen used with a proton pump inhibitor may also be safe. The American Geriatrics Society strongly recommends that older adults take only one NSAID at a time. Topical NSAIDs, however, are endorsed as adjuvants or alone (Gloth 2011).

Other NSAIDs, including indomethacin and ketorolac especially, are likely to cause significant toxicity in older patients. These drugs are highly protein bound, and older ill patients may have low levels of serum albumin. Older patients, therefore, are likely to have higher serum levels of free NSAID than do younger patients receiving the same NSAID dose, and they develop more side effects. Older patients with congestive heart failure or cirrhosis are particularly susceptible. Those taking NSAIDs may develop dizziness, confusion, and excessive salt and water retention. Since NSAIDs may exacerbate hypertension and can induce significant hyperkalemia and renal toxicity in this population, electrolytes and renal function must be checked a week or two after NSAID treatment is started. To minimize gastrointestinal toxicity, prescribe low-dose naproxen. But for patients requiring higher doses of this agent, or whose pain is well controlled only by NSAIDs with a higher risk of inducing gastrointestinal toxicity, add a proton pump inhibitor such as omeprazole (20 mg) and periodically monitor the patient with occult blood testing.

Other adjuvants also may cause significant side effects in older patients. Do not use diazepam (e.g., Valium). The increased body fat in these patients can prolong the half-life of lipid-soluble agents, such as diazepam, and lead to excessive sedation or delirium. Local anesthetics are also associated with a higher incidence of delirium in the elderly.

Avoid using tricyclic antidepressants. They can cause orthostatic hypotension, cognitive changes, and atrial arrhythmias, which can themselves be problematic or may lead to falls. If the patient does not tolerate even dose-reduced gabapentin (e.g., Neurontin) or pregabalin (Lyrica), try desipramine (Norpramin), which has the fewest anticholinergic side effects.

The anticholinergic side effects of the tricyclic antidepressants, the antiemetics, and the antihistamines (used to control opioid-induced pruritus) can be very troublesome. They include constipation, dry mouth, blurred vision, urinary retention, and sedation. Older opioid-naive patients also should not receive prophylactic phenothiazines.

Opioids. In general, because of the alterations in metabolism noted above, older patients are more likely to have significant side effects from the usual doses of both short-acting and sustained-release opioids. Given the same dose of opioid, older patients will have significantly higher plasma concentrations than younger patients. In addition, they are more sensitive to the peak effect of the immediate-release and short-acting preparations, and they can develop excessive respiratory depression, sedation, confusion, and even paradoxical agitation. With either short-acting or sustained-release formulations, the drugs last longer, their metabolites accumulate, and toxicities increase in these older patients.

Even short-acting opioids, such as immediate-release morphine, have long-lived active metabolites that may cause problems. Immediate-release hydromorphone (e.g., Dilaudid) or oxycodone pose less of a problem with metabolites. A transmucosal fentanyl product is another option, if the patient is opioid tolerant; the intermittent pains resolve in an hour or less, and insurance covers it. Avoid meperidine (e.g., Demerol). Older patients are particularly prone to the side effects of normeperidine, the active metabolite of meperidine, which causes dysphoria, myoclonus, and seizures.

To prevent excessive toxicity, "start low; go slow," and reassess frequently. Begin with a dose that is 25 to 50 percent less than the dose you would give to a younger adult. Rescue doses, which should be about 10 percent of the total daily dose in younger patients, initially should be no more than 5 percent in the older patient. Rescue medication, moreover, should probably be taken no more often than every 4 hours, rather than the every 2 hours recommended for younger patients.

Anecdotally, though I generally avoid long-acting and sustained-release opioids in this population, I have used 1 to 2 mg of methadone twice a day to good effect in patients over 80 who have neuropathic pain from nerve or skin lesions, like ischemic vascular ulcers.

Use lower doses of transdermal fentanyl in well-nourished older patients, because there is a marked increase in the transdermal delivery rate of the fentanyl. This may result from the higher fat-to-water ratio in the elderly person's skin, and more fentanyl may deposit in the skin reservoir than in that of younger patients.

For short-term relief of severe, acute pain, patient-controlled analgesia can be used as successfully in older patients as in younger persons. As in younger patients, the oral or transdermal routes are preferred for treating chronic cancer pain. If parenteral opioids are needed, it's best to avoid bolus injections because of the enhanced toxicity associated with the "peak effects." Continuous infusion via subcutaneous or intravenous routes is preferred. Intraspinal opioids can also be given safely. Older patients are less likely than younger patients to develop nausea or vomiting after an epidural injection.

Some special consideration must be given to opioid-induced side effects in older patients. As you might expect, older patients are more susceptible to the constipating effects of opioids. They are less active than younger patients, drink less fluid, have a more tolerant rectal sphincter, and are more often taking other medications that exacerbate constipation. It is therefore essential that older patients start a prophylactic bowel regimen along with opioid therapy.

Older patients are also prone to urinary retention due to the effects of opioids on the urinary sphincter. Urinary retention can be an important problem for patients with prostatic hypertrophy or those taking other drugs with anticholinergic side effects. Initially, these patients may require bladder catheterization to relieve discomfort, but the retention usually disappears after one to two days on opioid therapy. Rarely, patients with prostatic hypertrophy will require either a trial of finasteride or an agent that produces smooth muscle relaxation, such as terazosin (1 mg p.o. at bedtime, increased gradually to 2 to 5 mg as tolerated and as needed).

Relieving Pain in Substance Abusers

Active Abusers

The cancer patient who has severe pain but is actively abusing opioids, cocaine, or alcohol poses a difficult management problem. It is hard to trust the patient's report of pain intensity if you know he is actively abusing drugs, and you may be reluctant to prescribe a high opioid dose because you don't know whether you are relieving his pain or acting as his dealer.

Consider how Dr. William Breitbart, who has extensive experience working with substance abusers in pain, views this issue: "I've treated about 500 patients with AIDS-related pain and a history of substance abuse, and I've been fooled a good dozen times. But if I had allowed that experience of being manipulated and fooled to influence me, I would not have been able to help those other 488 patients" (personal communication). I share his sentiments; I would hate to miss

the opportunity to help so many people for fear that a few would be "using me" in ways I don't approve of.

I realize it is particularly hard to apply the assessment and management principles discussed thus far to this patient population. Unfortunately, we have no other way to assess or treat patients with severe pain: we must believe their reports of pain and try our best to bring it under control, even if they are actively abusing drugs.

To work with these patients, borrow the techniques used by the drug abuse professionals. Whenever possible, involve a team of clinicians to manage the case, including the patient's primary physician (or physician assistant or nurse practitioner), psychiatric clinicians, social workers, and drug abuse professionals. You might consider also involving a palliative care or pain specialist.

PRACTICE POINTS: OPIOID THERAPY FOR ACTIVE DRUG ABUSERS

- Control the environment.
- Establish the therapeutic opioid dose.
- Institute a regimen that minimizes the chance of abuse.

Inpatients. It is particularly important to control the environment of active drug abusers whenever they are admitted to an inpatient site. The patient should be in a private room and restricted to that room or, in some cases, to the floor. Patients should wear hospital, not street, clothing. Visitors (even family) should be restricted, and patients' possessions and packages should be searched by nursing staff. Arrange for frequent psychiatric or social work and substance abuse counseling, if you can, and try to have the same nurse responsible for the patient throughout the hospital stay (so-called primary nursing).

During the hospitalization, substitute therapeutic opioid doses for the opioids the patient was taking "on the street." Some former users, who now have cancer and are unable to get the medications they need from their physician, revert to using street drugs to self-medicate their severe pain. Your goal will be to demonstrate to them that you can relieve their pain with appropriate prescription agents and that they do not need the illegal substances for symptom control.

Finding the correct opioid dose may be particularly difficult in patients who are actively abusing opioids. You may not trust their reported pain level, and they often require very high levels of opioids (e.g., the equivalent of grams of morphine) for pain relief because of changes in their CNS created by their opioid abuse.

When you have brought the acute pain under control, you need to convert the patient to a regimen that minimizes the chance of abuse. Long-acting

oral agents such as levorphanol (e.g., Levo-Dromoran) or sustained-release preparations of morphine, hydromorphone (e.g., Exalgo), transdermal fentanyl, or methadone are recommended. Avoid immediate-release hydromorphone (e.g., Dilaudid), combination agents (e.g., Percodan, Percocet, Tylox), immediate-release morphine, and sustained-release oxycodone for patients who are active drug abusers.

Outpatients. After discharge, patients will need to continue to work with the psychiatric and substance abuse counselors to maximize compliance and to prevent recurrence of active abuse. The counselors can also provide education for the patients about the dangers of mixing the therapeutic opioids with alcohol.

Repeat your expectations of how patients are to work with you and your team, the psychiatric clinicians, and the drug abuse counselors. Be clear that if you are to continue to provide therapy for their cancer, they must continue to work with all those clinicians. Substance abuse is an illness that frequently relapses, and weekly urine checks are needed to identify recurrent substance abuse. Current technology can distinguish among a wide variety of opioid metabolites using both quantitative and qualitative methods. When you write prescriptions for the long-acting opioids, give only a week's supply at a time. And warn the patient to keep the medications in a safe place, as you will not replace that supply if it is accidentally "flushed down the toilet" or "spilled down the sink." If, despite all the support and repeated warnings, a patient continues to actively abuse opioids or other drugs, refer him to a different oncologist and give him only enough opioids to prevent withdrawal.

Rehabilitation in Remission: Mr. Salat

Substance abusers may be inspired to enter a rehabilitation program after their cancer goes into remission. Mr. Salat was such a patient. At the time I first saw him, he was 35 years old and had widely metastatic testicular cancer with lesions the size of grapefruits in his retroperitoneum and lung. He was actively abusing heroin, which he said helped him control the severe back pain caused by his retroperitoneal lesions. With ongoing support from his counselor and our office staff, he maintained pain relief throughout his treatment using only the opioids we prescribed.

When it was clear that his tumor was responding to treatment, I told Mr. Salat that when he was in complete remission, he was unlikely to need opioids for pain. I began to address his opioid dependence and my hope that he would be able to work with a drug counselor to avoid returning to his heroin use. He did not disap-

point me: he entered a methadone maintenance program and is still doing well in 2012, over twenty years later.

Patients on Methadone or Buprenorphine Maintenance

Alford and his colleagues (2006) suggest that clinicians have four main misconceptions about patients on methadone or buprenorphine maintenance: first, that their methadone or buprenorphine provides adequate pain relief; second, that if we use opioids to relieve their pain, we can cause their addiction to relapse; third, that they are at risk for sedation or respiratory depression if we treat their pain with additional opioids and continue their methadone or buprenorphine; and fourth, that they are just trying to manipulate us.

PRACTICE POINTS: OPIOID THERAPY FOR PATIENTS ON METHADONE MAINTENANCE

- Don't use methadone as the pain-relieving opioid. Leave the methadone dose unchanged and titrate other opioids to achieve pain control.
- Be aware that large opioid doses may be required for patients on significant doses of methadone.
- Maintain an ongoing relationship with the patient's drug counselor.

But in fact, patients on methadone maintenance present a less difficult compliance problem because they often have well-established, successful relationships with counselors. In addition to their methadone maintenance doses, however, they often require large doses of other opioids to relieve their pain (Doverty et al. 2001; Peles et al. 2005). You'll need to explain to the hospital staff or your office staff that these patients' reports of pain are just as reliable as those of nonabusers and that you plan to escalate the medications until their pain is relieved, whatever that takes. We have a number of options, according to Alford and colleagues, for patients on buprenorphine maintenance. These are described in detail in the paper by Alford, Comptom, and Samet that I've referenced at the end of this chapter.

For patients on methadone, reassure them that you will leave the methadone dose the same and use other opioids and adjuvant agents to relieve their pain (Alford et al. 2006). This allows patients to separate their drug abuse issues from their pain issues and helps them provide you with accurate pain assessments. Even PCAs may work in selected patients whose anxiety is decreased by their ability to have some control over their pain relief.

Former Abusers

People who have formerly abused opioids are often reluctant to take opioids, even for excruciating pain. They and their families remember the mess drug addiction made of their lives. They are terrified that if they take opioids to relieve their pain, they will again find themselves living that nightmare.

PRACTICE POINTS: OPIOID THERAPY FOR FORMER ABUSERS

- Be sensitive to the patient's and family's concerns about using opioids even for pain relief.
- Maintain an ongoing relationship with the patient's drug counselor.
- Monitor for signs of recurrent drug abuse.

Psychological support from a counselor familiar both with drug abuse issues and with opioids for pain management may be crucial to enabling patients to accept the pain medications they need for relief. Former abusers are very sensitive to being perceived as addicts, and staff members need to receive careful instruction in how to work with these patients to help them relieve their pain. Although relapse is uncommon in former abusers who suffer from cancer pain, they should still be monitored for signs indicating they have relapsed, such as "losing" medication, escalating doses without consulting you, obtaining medications from other physicians, or committing prescription fraud.

Physicians can relieve the pain of people who are actively abusing opioids, who are on methadone maintenance, or who formerly abused drugs. Patients will usually understand the need for the limits you set, or will at least comply with them in order to get pain relief. The teams you set up to support them may make it possible for them to "stay with the program." As long as you are aware of the potential pitfalls, and are vigilant, you will be able to prescribe opioids for substance abusers just as you do for nonabusing patients with the same goal: to free them from disabling pain.

Common Clinical Situations

Starting Patients on Opioids

As discussed in Chapter 2, starting patients on opioids can be unexpectedly difficult. Most patients and their families, at least initially, resist accepting a pre-

scription for opioids. To overcome their objections, I recommend conducting at least a ten-minute discussion in which you accomplish the following:

- Assume that patients and families are harboring the common fears and misconceptions about opioids, and dispel these fears.
- Explain the difference between tolerance and addiction, and affirm that they will not become addicts. Addicts use opioids "to get out of life"; patients use them to get back into their lives.
- Reassure them that taking medication now does not jeopardize achieving pain relief if the pain worsens ("there is plenty more where that came from").
- Using an analogy of the treatment of diabetes or heart failure, remind patients how opioids can help them reach their personal goals.
- Explain the likely side effects (e.g., constipation, sedation, nausea) and how you can prevent or treat these:
  - They may feel somewhat sleepy for the first two or three days, but the drowsiness will pass and the pain relief will remain.
  - Constipation will persist as long as they continue to take opioids, and it requires ongoing therapy. Advise them to replace any fiber laxatives with the laxatives you prescribe, to take them whether or not they have had a bowel movement that day, and to take more laxatives if they need them.
  - Nausea is not a sign of opioid allergy. It resolves over four to seven days and can be treated during that time if it is troublesome.

Initiating a treatment regimen for mild (level 1 to 4) to moderate (level 5 to 6) pain. For *mild* neuropathic pain, begin tramadol 25 to 50 mg orally or tapentadol 50 mg every 4 to 6 hours and titrate up as needed and tolerated. For patients with *mild* somatic or visceral pain, such as from bony metastases, begin with an NSAID such as acetaminophen or ibuprofen every 6 to 8 hours. If the pain relief remains unsatisfactory to the patient, either add low doses of a step 3 agent (i.e., morphine 7.5 mg, hydromorphone 2 mg, or oxycodone 5 mg) every 4 hours, or stop the acetaminophen or ibuprofen and add the step 2 agent immediate-release hydrocodone, which is only available in combination with acetaminophen or another NSAID (e.g., Vicodin). Give one or two combination pills every 4 to 6 hours.

For moderate pain (level 5 or 6 on a 0 to 10 scale), treat as follows:

- Begin with either (a) two of the combination hydrocodone and NSAID pills every 4 hours as needed, or (b) 15 mg of morphine, 4 mg of hydromorphone, 10 mg of oxycodone, 5 mg of oxymorphone, 50 mg of tramadol, or 50 to 100 mg of tapentadol orally every 4 hours as needed. For patients with somatic or visceral pain, add an NSAID such as acetaminophen or

ibuprofen every 6 to 8 hours. Add one or two stool softeners and one or two senna tablets twice a day (or choose another laxative from Table 6.6). If the pain is neuropathic, do not use an NSAID as an adjuvant to the opioid. Instead add gabapentin 100 mg orally three times a day and titrate to a therapeutic level, at least 300 mg orally three times a day, over several weeks.

- Identify a pain scale that the patient and family feel comfortable using. Ask the patient to record, at least twice a day, her pain level before and about one hour after she takes the drug, along with any side effects.
- The day after each opioid dose change, check with the patient to determine whether the pain relief is now satisfactory.
- If the pain relief is satisfactory but the patient has developed side effects, treat them as described earlier in this chapter.
- If the pain is relieved for only one or two hours and pain recurs before the next dose, start an equivalent amount of a sustained-release (SR) morphine, hydromorphone, hydrocodone, oxycodone, oxymorphone, or fentanyl preparation, adding an immediate-release (IR) form for pain between regularly scheduled doses (rescue doses). The rescue dose should be 10 percent of the total daily opioid dose (5 percent initially in older patients). It is sometimes necessary to "round up" or "round down" the calculated opioid dose to accommodate the dosages available in SR or IR preparations. I give examples of how to do these calculations later in the chapter. If appropriate, continue the gabapentin for neuropathic pain, the NSAID, or add an amount of NSAID equivalent to the amount in the combination tablet that the patient formerly took.

TREATING PAIN THAT RECURS BEFORE THE NEXT DOSE

Converting from a combination product to acetaminophen or NSAID + a sustained-release form of the same opioid (oxycodone):

- Initial combination agent: oxycodone (5 mg) + acetaminophen, 12 tablets per 24 hours (2 tablets every 4 hours).
- Total oxycodone dose: 5 mg/tablet × 12 tablets = 60 mg.
- Equivalent SR oxycodone: 30 mg every 12 hours.
- Add opioid rescue dose (10 percent of 24-hour dose): 10 percent of 60 mg ≈ 5 mg of IR oxycodone.
- Add back acetaminophen or NSAID if needed.

Initial opioid regimen for opioid-naive outpatients with severe (level 7 to 10) pain. The step 3 opioids are indicated for initial therapy of patients with severe pain. They include hydromorphone (e.g., Dilaudid) for older patients or for patients with renal or hepatic failure, as well as morphine, oxycodone, and oxymorphone. Begin with the starting doses listed in Table 6.4. Unless you're using the intravenous route, do not use fentanyl for initial therapy for a patient in severe pain; it takes 12 to 20 hours to achieve a therapeutic level of fentanyl after the patient applies a fentanyl patch. Because of the concerns described earlier in this chapter, do not use methadone as the initial agent, unless you are experienced in its use. Some patients need to be admitted to bring their pain under control. Later in the chapter, I review how to treat such a patient, whom I consider to be in a pain crisis.

TREATING PAIN THAT IS UNRELIEVED BY A STEP 2 AGENT

Converting from a combination agent to a sustained-release preparation containing the same opioid (oxycodone) at a higher dose:

- Initial combination agent: oxycodone 5 mg + acetaminophen, 12 tablets per 24 hours (60 mg of oxycodone) (2 tablets every 4 hours).
- Increase the oxycodone by 50 percent: 60 mg + (60 mg × 50 percent = 30 mg) = 90 mg of oxycodone ≈ 40 mg of SR oxycodone every 12 hours.
- Adjust rescue dose of oxycodone: 10 percent of 80 mg ≈10 mg; rescue dose: 10 mg of IR oxycodone every 2 hours p.r.n.
- Add back acetaminophen or NSAID if needed.

Whichever opioid you choose, prevention of constipation is crucial. Prescribe, for example, two senna plus two Colace twice daily with an osmotic agent (e.g., 17 g of polyethylene glycol [Miralax]) at bedtime; exclude the osmotic agent if it causes diarrhea. Instruct all patients to take the laxatives even if they have had a bowel movement that day.

For patients with moderate to severe neuropathic pain, add gabapentin taken three times a day (e.g., 100, 100, 300 mg p.o.). If the pain is very severe, consider also adding a steroid taper, using an initial dose of 8 mg oral dexamethasone taken before noon, followed by 4 mg twice daily for 2 days, 2 mg twice daily for two days, and 2 mg a day for two days. If the gabapentin is well tolerated, increase the dose over several weeks until pain relief is improved or the patient has a dose-limiting side effect. If the gabapentin is ineffective at 300 mg taken orally three times a day, switch to pregabalin; if this is ineffective add to it another of the anticonvulsants listed in Table 6.10.

Changing Opioid Dose, Opioid Agent, or Route of Delivery

Adjusting the dose. The initial dose of opioid is, unfortunately, no better than an educated guess. Doses often need to be adjusted upward or downward both during the first few weeks of therapy and later in the patient's course of treatment, as the disease process advances. Explain this to patients, and ask which is preferable to them: rapidly relieving the pain or avoiding side effects such as sedation. If patients and their families want immediate pain relief regardless of the side effects, I am comfortable with using a higher initial dose. If they express a great deal of concern about the potential side effects, I am more conservative with the initial dose, but I supply rescue medication, carefully monitor the patient, and raise the dose until the relief of the constant portion of the pain is satisfactory. Ideally, patients with constant, not intermittent, pain need to use rescue doses of IR opioids only once or twice a day; the bulk of the pain relief should be provided by the SR opioid. Patients without constant pain, whose pain is intermittent incident pain, will benefit most from taking IR opioids when they have pain. SR opioids may cause excessive sedation in these patients.

INITIAL ORAL OPIOID FOR OPIOID-NAIVE PATIENTS WITH SEVERE PAIN

- Hydromorphone 4 to 6 mg p.o. every 4 hours for elderly patients or patients with renal or hepatic failure.
- IR options: IR morphine or oxycodone every 2 hours p.r.n. for 24 hours; then give total daily dose in SR form.
  Example.
  7.5 mg IR morphine (½ of a 15-mg tablet) × 12 doses = 90 mg of morphine.
  SR dose: 45 mg q12h SR morphine with 10 mg IR morphine rescue (e.g., 0.5 ml of a 20 mg/ml morphine solution).
  Example.
  5 mg IR oxycodone × 10 doses = 50 mg oxycodone.
  SR dose: 20 mg q12h SR oxycodone with 5 mg IR oxycodone rescue (alone or in combination with aspirin, acetaminophen, or NSAID).
- SR option
  Example.
  Morphine SR 30 mg p.o. q12h or oxycodone SR 20 mg q12h with 5 mg IR oxycodone rescue (alone or in combination with aspirin, NSAID, or acetaminophen).

INITIAL TRANSDERMAL FENTANYL FOR OPIOID-NAIVE PATIENTS WITH SEVERE PAIN

- Initial dose of transdermal fentanyl: 25 µg/hr patch, which is approximately equivalent to 50 mg of morphine every 24 hours. (Patients taking 7.5 mg of IR morphine every 4 hours, take a total of 45 mg of IR morphine in 24 hours.)
- Add rescue doses of 10 mg of IR morphine or oxycodone (0.5 ml of a 20 mg/ml solution) every 2 hours p.o. or sublingual p.r.n.
- Patients should expect to use rescue doses until fentanyl blood levels are adequate (i.e., for at least the first 12 to 24 hours after receiving the patch).

USING RESCUE DOSES TO INCREASE SUSTAINED-RELEASE OPIOID DOSE FOR PATIENTS WITH CONSTANT PAIN

Example.

A patient taking 45 mg of SR morphine every 12 hours took six rescue doses, 10 mg each, of IR morphine (0.5 ml of a 20 mg/ml morphine solution).

Total morphine dose taken in 24 hours: 90 mg + 60 mg = 150 mg.

New SR morphine dose: 75 mg every 12 hours; rescue dose: 15 mg IR morphine.

To safely escalate the opioid dose in a patient with constant pain after the patient has been taking an SR preparation for 24 to 48 hours,

- Ask the patient to record all rescue doses he takes.
- If the total amount of drug he takes as a rescue dose is more than 25 percent of the total SR dose, increase the SR dose by the amount in the rescue doses.

Changing opioid agents. Patients commonly need to change opioid agents because of intolerable side effects. Much has been written about the challenges of making these changes, given that the equianalgesic tables we use are far from perfect (Knotkova et al. 2009; Fine et al. 2009). Using an equianalgesic table such as the one provided in this chapter (Table 6.5) will give you somewhere to start; you should be able change agents safely while maintaining adequate

control of the patient's pain. I always let patients know that this is an inexact science, and that they're likely to be either more sedated or in more pain than they'd like to be for the first few days as we work to get the dose of the new agent adjusted. Knowing which of these they can tolerate (sleepiness or uncontrolled pain) helps me know where to start in the range of "acceptable" doses of the new opioid.

In Table 6.5, the columns indicate the equianalgesic oral and parenteral opioid doses for the listed drugs. For example, 30 mg of oral IR morphine equals 20 mg of oral IR oxycodone or 7.5 mg of oral hydromorphone (e.g., Dilaudid). And 10 mg of parenteral morphine equals 1.5 mg of parenteral hydromorphone.

Some patients will never achieve pain relief from a fentanyl patch. An adequate fat reservoir cannot form in patients who are very thin or have arm edema or extensive arm tattoos. Patches may not adhere because of skin oils or sweat. If you wish to change the treatment to an oral or intravenous opioid, the safest way to do this in these patients is to assume the patients are not absorbing *any* of the fentanyl and to base your calculation on the amount of rescue opioid they have taken in the past 24 to 48 hours.

It is impossible to tell how much fentanyl the patient might be absorbing from the skin reservoir, so I make the conversion the same way I would if I thought the patient was receiving a full fentanyl dose from the patch. I give only immediate-release rescue opioid as needed for the first 6 hours after the patch is removed. For the next 6 hours, you can give standing parenteral or oral SR opioids at a dose that is only 50 percent of the full, calculated dose. After 12 hours, you can begin the full, calculated dose.

For example, consider a very thin patient who is not getting adequate relief from a 200-μg/hr fentanyl patch placed on the chest wall and has used 24 mg of IV hydromorphone in the previous 24 hours for pain relief. I assume that without the patch, she'll need at least 1 mg/hr hydromorphone (24 mg / 24 h) for pain relief. After taking off the patch, I would give that patient 2 to 3 mg of IV hydromorphone or 12 to 16 mg of oral hydromorphone every 2 hours as needed for the next 6 hours. I would then start a hydromorphone drip at 0.5 mg/hr for the next 6 hours or continue the oral hydromorphone. Twelve hours after the patch is removed, I would increase the drip to 1 mg/hr.

Some patients may develop an allergy to the adhesive in the patch. If such patients were taking fentanyl because they poorly tolerated other opioids, the fentanyl can be given as an SQ or IV infusion at the same rate as the patch (Hough 2003).

CONVERTING FROM SUSTAINED-RELEASE MORPHINE TO SUSTAINED-RELEASE OXYCODONE

Example.

Current SR morphine dose: 60 mg p.o. every 12 hours (total dose: 120 mg / 24 hr).

Equivalent SR oxycodone dose: 40 mg every 12 hours (total dose: 80 mg / 24 hr).

⅔ × 80 mg = 55 mg

New SR oxycodone dose: 30 mg every 12 hours; rescue dose: 5 mg IR oxycodone.

CONVERTING FROM SUSTAINED-RELEASE MORPHINE TO EXTENDED-RELEASE HYDROMORPHONE

Example.

Current SR morphine dose: 60 mg p.o. every 12 hours (total dose: 120 mg / 24 hr).

Equivalent p.o. hydromorphone (e.g., Dilaudid) dose: (120 mg / 30) × 7.5 = 30 mg.

⅔ × 30 mg = 20 mgNew hydromorphone dose: 24 mg extended-release p.o. every 24 hours (or 4 mg IR every 4 hours); rescue dose: 2 mg IR hydromorphone.

At the bottom of Table 6.5 the data apply only to equivalencies between fentanyl (delivered by transdermal fentanyl patch in micrograms per hour) and the total amount of parenteral or oral morphine taken in 24 hours. For example, the equivalent morphine dose for a patient with a 50 μg/hr fentanyl patch is 33 mg of intravenous morphine in 24 hours, or 100 mg of oral morphine in 24 hours. Similarly, the equivalent fentanyl dose for a patient on an intravenous morphine drip of 4 mg/hr (i.e., 96 mg in 24 hours) is 150 μg/hr.

Except when converting from fentanyl to morphine or vice versa (Table 6.5), it is not sufficient simply to calculate the equianalgesic dose of the new opioid. Patients who take an opioid for several weeks become tolerant to many of the side effects that opioid induces, but they may not be as tolerant to the side effects caused by the new drug. If their pain is well controlled and they take a full equianalgesic dose of the new opioid, they may develop significant sedation or respiratory depression. To take into account this "incomplete cross-tolerance" between opioids, in patients with well-controlled pain, prescribe about *two-thirds* of the calculated equianalgesic dose of the new opioid. If the pain is not adequately relieved,

however, give the full equianalgesic dose of the new agent. In all cases, 10 percent of the 24-hour dose of the new opioid becomes the new rescue dose. For very large doses of oral opioid, reduce the starting dose of the other agent by half.

CHANGING AGENTS WHEN THE OPIOID DOSE IS HIGH

Example.
A patient takes 600 mg of sustained-release oral morphine every 12 hours (1200 mg every 24 hours).

Hydromorphone:
Equivalent: (1200 mg / 30) × 7.5 = 300 mg. New dose: 300 mg / 2 = 150 mg / 24 hr.

SR oxycodone:
Equivalent: (1200 mg / 30) × 20 = 800 mg. New dose: 800 mg / 2 = 400 mg / 24 hr.

Transdermal fentanyl (extrapolation from available data)*:*
Equivalent: 600 µg/hr. New dose: 300 µg/hr transdermal fentanyl patch.

It is much more difficult to convert patients safely to methadone, especially from high doses of other opioids. As I discussed earlier in this chapter, the equianalgesic ratios change as the non-methadone opioid dose increases. Values range from a ratio of 4:1 at morphine equivalents of less than 100 mg daily, to 20:1 at morphine equivalents of greater than 1000 mg daily. First, determine the morphine equivalent of the average total amount of opioid the patient has taken daily for the previous two days (a discussion of how to do this appears later in this chapter). If the total morphine equivalent was 300 mg on the first day and 400 mg on the second, the average total daily amount would be 350 mg; use that amount to determine the methadone dose according to the ratios in the box below:

MORPHINE EQUIVALENT METHADONE DOSES

Oral Morphine Equivalent (mg/24 h)	*Morphine: Methadone Ratio*
<100	4:1
101–300	8:1
301–600	10:1
601–800	12:1
801–1000	15:1
>1000	20:1

After using this table to calculate the equianalgesic dose of methadone, decrease that calculated dose by 50 percent, because of methadone's inhibition of the NMDA receptor (see discussion above), and give it in divided doses, usually three times a day. I describe in detail earlier in the chapter how to convert a patient from oxycodone to methadone. If you have questions about this conversion procedure, consult a palliative care or anesthesia pain specialist.

Changing the route of delivery. Even changing from the oral to the parenteral route of the *same* agent necessitates a change in opioid dose. A large proportion of an oral opioid dose is metabolized in its first pass through the liver, and these metabolites cannot cross the blood-brain barrier to provide pain relief.

CHANGING FROM OXYCODONE TO METHADONE

Example.

A patient takes 200 mg of sustained-release oral oxycodone every 8 hours (600 mg every 24 hours)
600 mg oral oxycodone = 900 mg oral morphine
Morphine to methadone ratio: 15:1
Equianalgesic methadone dose: 900 mg / 15 = 60 mg of methadone
Decrease calculated methadone dose by 50 percent because of NMDA activity of methadone:
30 mg methadone
New dose: 10 mg p.o. q8h, beginning day 1

Day 1: Give 200 mg of sustained-release oxycodone q8h and 10 mg of methadone q8h and 60mg IR oxycodone as needed q4h if the patient complains of pain
Day 2: If the patient has used 3 or fewer doses of prn IR oxycodone, give 100 mg of sustained-release oxycodone q8h and 10 mg of methadone q8h and 60mg IR oxycodone as needed q4h if the patient complains of pain.
—Patient takes two 60-mg doses during the 24 hours.
Day 3: Stop sustained-release oxycodone. Continue 10 mg of methadone p.o. q8h and 60mg IR oxycodone as needed q4h if the patient complains of pain.

SOME COMMON ORAL-TO-PARENTERAL OPIOID CONVERSIONS

Morphine: ratio of oral dose to parenteral dose = 3:1

Example.
Oral dose: 360 mg q12h; 24-hour total dose = 720 mg p.o.
Equivalent IV/SQ dose: 720 mg p.o. / 3 = 240 mg / 24 hr IV (i.e., 10 mg/hr).

Hydromorphone: ratio of oral dose to parenteral dose = 5:1

Example.
Oral dose: 12 mg every 4 hours; 24-hour total dose = 72 mg p.o. Equivalent IV/SQ dose: 72 mg p.o. / 5 ≈ 14 mg / 24 hr IV or SQ (i.e., 2.3 mg IV every 4 hours or 0.6 mg/hr). Round to nearest dose that can be administered: 2–2.5 mg IV every 4 hours.

House staff need to be reminded that it's very important to specify the route by which the opioid should be given. I was once called by the nurses because a house officer had written an order for "6 mg of hydromorphone IV or p.o. q4h." The patient had been taking the oral hydromorphone dose but was going to be NPO for surgery. Luckily, the nurse did not give the 6 mg intravenous bolus; if she had, the patient would have received the equivalent of 30 mg of oral hydromorphone.

Converting from Multiple Oral Agents to a Single Parenteral Agent. While converting from an oral to a parenteral route of the same opioid is fairly straightforward, other conversions can be more challenging. Not infrequently, when patients are admitted to the hospital, they are taking several different oral opioids, and these must be converted to a single parenteral medication. To start a drip using morphine, I calculate the patient's total daily oral opioid dose in morphine equivalents, reduce the doses of other opioids by one-third to adjust for incomplete cross-tolerance, add all the morphine equivalents together to get the total oral morphine equivalent for 24 hours, and divide that total by 3 to get the total intravenous morphine equivalent over 24 hours. Finally, I divide that total by 24, which becomes the continuous-infusion rate for the intravenous morphine.

Here are two sample calculations of patients whose pain control is satisfactory, but who need to be switched from oral to parenteral opioids. The first is a patient with myeloma who broke her femur and needed to have a pin placed before she received radiation (see "Converting from IR Oxycodone plus SR Morphine to an Equivalent Parenteral Morphine Dose"). She would be NPO in

the perioperative period. She had been taking 60 mg of SR morphine every 12 hours, with two 5 mg oxycodone every 4 hours as needed for breakthrough pains. Since the fracture, she had in fact taken twelve oxycodone tablets a day in addition to the morphine.

The second is a patient who was taking 180 mg of SR oxycodone a day and hydromorphone for rescue (see "Converting from IR Oxycodone plus SR Morphine to an Equivalent Parenteral Morphine Dose"). He took 24 mg of oral hydromorphone on the day before admission. Intravenous hydromorphone could be used, but for this example, assume that you wish to prescribe morphine.

CONVERTING FROM IR OXYCODONE PLUS SR MORPHINE TO AN EQUIVALENT PARENTERAL MORPHINE DOSE

- Calculate oral morphine equivalents taken in the past 24 hours and decrease doses of other opioids by one-third to adjust for incomplete cross-tolerance.

Current Medications	*Oral Morphine Equivalents*
IR oxycodone 60 mg	60 mg (i.e., 90 mg – 30 mg)
SR morphine 120 mg	120 mg
Total	180 mg oral morphine@BTB:

- Calculate the IV morphine drip rate.

Oral Morphine	*Parenteral Dose*	*IV Drip Rate*
180 mg	60 mg (180 mg / 3)	2.5 mg/hr (60 mg / 24 hr)

Some patients are admitted with persistent pain despite taking oral opioids. Because their opioid doses should be increased, I do not decrease the equianalgesic dose for "incomplete cross-tolerance." I give them the exact equivalent in morphine, which, in effect, is a 33 percent increase in dose. For example, you might want to start an intravenous morphine drip for a patient whose average pain intensity is 6 despite taking two, 5 mg oxycodone every 4 hours (i.e., 10 mg oxycodone × 6 doses = 60 mg IR oxycodone) and 60 mg of SR oxycodone every 12 hours.

If you are converting a patient from oral to parental opioids who has not received intravenous opioids before, it is important to explain to him why you are using this route. I learned this from a young patient with testicular cancer who was admitted with severe retroperitoneal pain caused by metastases.

CONVERTING FROM ORAL SR OXYCODONE PLUS HYDROMORPHONE TO AN EQUIVALENT PARENTERAL MORPHINE DOSE

- Calculate oral morphine equivalents taken in the past 24 hours and decrease doses of other opioids by one-third to adjust for incomplete cross-tolerance.

Current Medications	*Oral Morphine Equivalents*
SR oxycodone 180 mg	180 mg (i.e., 270 mg − 90 mg)
Hydromorphone 24 mg oral	64 mg ([{24 mg / 7.5} × 30] − 32)
Total	244 mg oral morphine

- Calculate the IV morphine drip rate.

Oral Morphine	*Parenteral Dose*	*IV Drip Rate*
244 mg	81 mg (244 mg / 3)	3.4 mg/hr (81 mg / 24 hr)*

*Round to nearest dose that can be administered: 3.5 mg/hr.

Dire Implications of a "Morphine Drip"

Joe was an 18-year-old student whose family physician had discovered a testicular mass several months before. Joe had insisted that he wanted to finish the school year before having any diagnostic procedures. He made it through graduation but soon after was admitted for pain control from extensive painful retroperitoneal adenopathy.

To relieve his pain I suggested a morphine drip with morphine boluses as needed. When I next went to see Joe, he was in tears. I asked what was the matter, and he replied, "I knew from Dr. Porter that I was sick, but he never told me I was about to die!" I was taken aback and told him that, on the contrary, he had every chance of being cured by the chemotherapy. When I asked what had made him think he was terminally ill, he said, "Well, the nurses told me you started a morphine drip. And the only time I ever heard of that being used was on my Aunt Jane; they started one on her just a few days before she died."

Since this experience, I have been careful to explain to a patient why I am choosing intravenous opioids, saying something like,

I know you are having very severe pain and I want to lower the level of the pain as fast as I can. To do this, I need to give you opioid medications, like morphine, and I need

CONVERTING FROM ORAL IR AND SR OXYCODONE TO A PARENTERAL MORPHINE DOSE FOR A PATIENT IN PERSISTENT PAIN

- Calculate oral morphine equivalents taken in the past 24 hours.

Current Medications	*Oral Morphine Equivalents*
IR oxycodone 60 mg	90 mg
SR oxycodone 120 mg	180 mg
Total	270 mg oral morphine

- Calculate the IV morphine drip rate.

Oral Morphine	*Parenteral Dose*	*IV Drip Rate*
270 mg	90 mg (270 mg / 3)	3.75 mg/hr* (90 mg / 24 hr)

*Round to nearest dose that can be administered: 3.5 to 4 mg/hr

to give them intravenously. This doesn't mean you're about to die; it's just that this is the fastest way I can bring your pain under control. As soon as I know what dose of opioids you need, I'll switch you to oral medications.

I have frightened many fewer patients since I adopted this technique.

Changing from Pills to a Transdermal Fentanyl Patch and Vice Versa. The technique for changing patients from oral medications to a transdermal fentanyl patch includes not only determining the equianalgesic dose (Table 6.5) but also providing pain relief during the time it takes for the patch to begin providing adequate analgesia. This is very easy to do if the patient is taking an SR morphine or oxycodone preparation. Avinza relieves pain for 24 hours, Kadian relieves pain for 12 to 24 hours, and the other SR preparations relieve pain for about 12 hours, which is almost the same amount of time it takes for the patch to begin providing adequate pain relief. Therefore, instruct the patient to take the last dose of the SR opioid pills (or 50 percent of the Avinza dose) at the time she applies the first patch and to use the rescue doses if needed. If, 72 hours after the patch is placed, the patient's pain control is not satisfactory or her rescue doses exceed 25 percent of the total daily opioid dose, increase the dose of the fentanyl patch by an amount equivalent to the amount of rescue medication taken. Further dose titrations may be needed over the ensuing weeks.

To convert from a fentanyl patch to oral medications, you must take into consideration the significant amount of fentanyl that remains in the skin reservoir

after the patient has removed the patch. Therefore, ask the patient to refrain from taking the usual scheduled opioid for the first 12 hours after the patch is removed and instead to take rescue medication if pain recurs. At 12 hours after patch removal, since the skin reservoir is still half full, the patient should take half the equianalgesic dose of the oral opioid agent. Twenty-four hours after the patch is removed, the patient may resume taking the full equianalgesic dose of oral opioid.

CONVERTING FROM ORAL OPIOIDS TO TRANSDERMAL FENTANYL

Example.

A patient taking SR morphine 150 mg p.o. every 12 hours would like to switch to transdermal fentanyl.

Refer to Table 6.5 for the fentanyl dose that should be prescribed for each oral morphine dose. A further one-third decrease is not required.

Current Medications	*Transdermal Fentanyl Equivalents*
SR morphine 300 mg	150 µg/hr

Rescue dose: 30 mg IR morphine

Give the last dose of 150 mg of SR morphine at the time the patch is placed.

INCREASING THE DOSE OF TRANSDERMAL FENTANYL

Example.

A patient who had been maintaining excellent pain relief using a 75 µg/hr fentanyl patch (equivalent to 150 mg of morphine) had for the past three days required six 15-mg doses daily (total 90 mg) of IR morphine (i.e., about 33 percent of the total daily opioid dose) for increased pain.

Refer to Table 6.5 for the fentanyl dose equivalent to the oral morphine dose.

Current Medications	*Transdermal Fentanyl Equivalents*
Fentanyl 75 µg/hr	75 µg/hr
IR morphine 90 mg	45 µg/hr
New patch strength	125 µg/hr (closest dose to patches available)

Calculate new rescue dose.

Fentanyl Dose	*Morphine Equivalent*
125 µg/hr	250 mg
Rescue dose	10 percent of 250 mg ≈ 30 mg IR morphine

CONVERTING FROM A TRANSDERMAL FENTANYL PATCH TO ORAL OPIOID

Example.

A patient using a 100 μg/hr transdermal fentanyl patch is to be switched to the equivalent SR morphine dose.

Referring to Table 6.5, select the equianalgesic dose.

Current Fentanyl Dose	*Morphine Equivalent*
100 μg/hr	200 mg morphine / 24 hr

Rescue dose: 20 mg IR morphine (e.g., 1 ml of a 20 mg/ml elixir)

- Patient removes the patch; takes IR morphine every 2 hours p.r.n. for the next 12 hours.
- Twelve hours later, the patient takes 45 mg of SR morphine (≈50 percent of 100-mg dose).
- Twelve additional hours later, 24 hours after removing the patch, the patient begins 100 mg of SR morphine every 12 hours.

Rapidly Relieving Excruciating Pain

Rarely, you will admit a patient who has a pain "emergency": the pain has been severe (≥7 on a scale of 0 to 10) for at least six hours and has escalated over the past several days. The patient is in agony, and you want to relieve the pain as soon as possible. You can do this most expeditiously using morphine or hydromorphone intravenous bolus doses. To do this safely, however, the patient must be monitored very closely. While the bolus doses are being given, the patient should be under continuous observation, with recordings at least every 15 minutes of vital signs, continuous pulse oximetry, verbal pain scores, mental status changes (e.g., using the Richmond Agitation Sedation Scale [RASS]), and other adverse events, until the pain level has fallen to less than 5. This process usually takes several hours.

Rapid dose escalation is usually needed to overcome severe pain in both opioid-naive patients and patients who are already taking opioids. In both situations, prescribe a bowel regimen and ensure close monitoring for opioid-induced nausea and sedation. With careful patient observation, opioid doses can be increased substantially without excessive toxicity. Suggestions for dosing of IV boluses and recommended monitoring parameters for both types of patients are given in the boxes describing the treatment of severe pain.

TREATING SEVERE PAIN (GREATER THAN 7/10) IN AN OPIOID-NAIVE PATIENT

- Begin a bowel regimen; monitor the patient for nausea/sedation due to opioids.
- PCA option
  - —Begin with loading dose, basal rate, and bolus dosing.
    Hydromorphone for patients with renal failure:
    0.2 to 0.5 mg loading dose + 0.01 mg/kg basal rate + 0.2 to 0.4 mg boluses every 7 minutes p.r.n.
    Sample calculation. For a 70-kg man, hydromorphone basal rate = 0.7 mg/hr. For very elderly patients or patients with CO_2 retention, begin at 0.35 mg/hr.
    Morphine for other patients:
    2 to 5 mg loading dose + 0.05 mg/kg basal rate + 2 to 4 mg boluses every 7 minutes p.r.n.
    Sample calculation. For a 70-kg man, morphine basal rate = 3.5 mg/hr. For very elderly patients or patients with CO_2 retention: begin at 0.25 mg/hr.
  - —Check vital signs including level of sedation every 15 minutes
  - —Reevaluate pain hourly.
  - —Double bolus doses every hour until pain level falls below 5 or becomes tolerable.
  - —Increase the basal rate every 12 hours as needed, adjusting rate by the p.r.n. opioids received.
    Example.
    A patient receiving 3 mg/hr IV morphine received 24 mg IV morphine over the past 12 hours. About 12 of 24 mgs is not yet metabolized.
    New IV morphine basal rate: 3 mg/hr + 12 mg / 12 hr = 4 mg/hr
- IV bolus option
  - —Give 5 to 10 mg of IV morphine over 15 minutes; evaluate vital signs and pain relief 15 minutes after the infusion is complete.
  - —If pain level is unchanged, double the bolus dose; check vital signs; reevaluate pain 15 minutes after this bolus fusion is complete. If still unchanged, repeat.
  - —When pain level decreases but is still ≥5, repeat the same bolus dose; check vital signs; reevaluate pain level 15 min after this bolus infusion is complete. If still ≥5, repeat.

(continued)

—When pain level <5, give the effective bolus dose q2h as needed for next 12 hours.

—When pain control is adequate, begin continuous infusion or oral or transdermal opioid based on the opioid used in the past 12 hours.

Example.

Morphine to reduce pain level to <5: 35 mg over 2 hours (5 mg + 10 mg + 20 mg).

Three additional 20-mg boluses required in the next 6 hours. Total morphine taken in 8 hours: 95 mg IV. Because the half-life of morphine is 4 hours, 50 percent of the 95 mg will have been metabolized.

Options: morphine drip at 6 mg/hr (47.5/8) or oral or transdermal opioid equivalent to 6 mg/hr parenteral morphine with 10 mg IV morphine q2h p.r.n. rescue.

A more rapid titration of morphine (2 mg IV every 2 minutes) has been found effective in decreasing the excruciating pain of both opioid-naive and opioid-tolerant patients to a tolerable level (<4) within 15 minutes (Mercadante et al. 2002). The majority of patients (30 of 45) were not receiving morphine prior to the onset of the excruciating pain. Doses required to achieve pain levels of less than 4 were modest (mean dose of 8.5 mg, Confidence Interval 6.5 to 10.5 mg IV morphine). Doses of up to 40 mg IV were given, and no significant adverse events noted.

Another report demonstrated that a rapid titration of intravenous fentanyl could control severe pain in as little as 10 minutes (Soares et al. 2003). The patients did not have neuropathic pain, and all had been taking morphine for at least two weeks before the pain emergency occurred. The fentanyl dose was calculated from the previous morphine dose, using 10 percent of the previous 24-hour opioid dose and a ratio of 1 mg morphine to 10 μg fentanyl. For example, if a patient was taking 150 mg/day of oral morphine, the IV morphine equivalent is 50 mg/day; 10 percent of that is 5 mg IV morphine. The equivalent fentanyl dose is 50 μg. The patient would receive a 50 μg fentanyl bolus. If the pain remained at 4 or higher after 5 minutes, a second 50 μg bolus was given; if the pain remained at 4 or higher after an additional 5 minutes, the fentanyl dose was increased by 50 percent. The last dose (i.e., 75 μg) could be given again 5 minutes later if necessary. All 18 patients treated were carefully monitored in the emergency department, and all had relief of pain, with an average time to control of 11 minutes, and without adverse effects.

TREATING SEVERE PAIN IN A PATIENT ALREADY TAKING OPIOIDS

- Continue the bowel regimen; monitor the patient for nausea or sedation caused by the increased opioid dose.
- IV bolus option. Continue the previous oral SR or transdermal opioid; add additional opioid by IV bolus every 30 minutes to an hour, depending on the monitoring available.
  - —Double the bolus dose if the pain is >7; give the same dose if the pain is >4.
  - —Check vital signs every 15 minutes.
  - —Reevaluate the pain level 30 minutes after each dose is given.
  - —When the pain has been brought under control, adjust the oral/transdermal dose by the amount of rescue opioid required.

    Example.

    Sustained-release oral morphine: 100 mg every 12 hours.

    Current rescue dose: 15 mg IR morphine every 2 hours p.o. = 5 mg every 1 hours IV.

    IV rescue doses over the first 4 hours: 5 + 10 + 10 = 25 mg IV morphine.

    Total IV rescue doses (mg) over 12 hours: 50 mg IV morphine = 150 mg oral morphine. Add 50% of that to the basal opioid dose.

    New oral morphine dose: 100 + 75 = 175 mg sustained-release oral morphine every 12 hours.

    New rescue dose: 30 mg IR morphine p.o. q2h p.r.n.
- PCA option.
  - —Start IV morphine PCA with basal rate at twice the current rescue dose.

    Basal rate: 10 mg/hr IV morphine, with boluses of 5 mg morphine IV every 7 minutes p.r.n.
  - —Reevaluate vital signs, including sedation, every 15 minutes, pain hourly.
  - —Double bolus doses every hour until pain level falls below 5 or becomes tolerable. Continue the effective bolus dose.
  - —Increase the basal rate every 12 hours p.r.n., adjusting for bolus doses taken and half-life of morphine.

    Example.

    A patient receiving 10 mg/hr IV morphine required 12 boluses of IV morphine in the past 12 hours (5 mg + 10 mg + [20 mg × 10]).

    New basal rate: 10 mg/hr + 215 mg/12 hr = 28 mg/hr / 2 = 14mg/hr.

When satisfactory pain relief is finally achieved, the patient usually falls asleep. This is not a signal to decrease the opioid drip rate. The patient is not overdosed; he is simply exhausted by loss of sleep due to the excruciating pain. If the patient is difficult to arouse, hold the drip for an hour and then restart it at 50 percent of the previous dose. When the patient awakens, continue careful evaluations of pain intensity and side effects. Once the pain has been controlled for a day or two, the patient is likely to require less opioid to maintain the same level of pain relief.

Patients who are opioid tolerant who develop excruciating somatic pain are likely to respond to infusions of hydromorphone, with bolus doses both to establish an initial level and to provide rescue for incompletely relieved pain. Calculate an equianalgesic starting dose from the opioids the patient has been taking that have not relieved her pain, and do not decrease for incomplete cross-tolerance, because you know the patient needs a 50 to 100 percent increase in opioids because of her severe pain.

Susannah, for example, was a 35-year-old woman with metastatic breast cancer and increasing bone pain who had been taking 100 mg of sustained-release morphine every 8 hours when her pain level "got out of control." She had taken six 30-mg rescue doses in the past few days without relief. Her total oral morphine per day was, therefore, 300 mg + 180 mg = 480 mg. Knowing that 30 mg of oral morphine is equivalent to 1.5 mg of IV hydromorphone, to calculate her drip rate, I divided 480 mg by 30 = 16 and multiplied that by 1.5 = 24 mg of IV hydromorphone per 24 hours, or 1 mg/hour. I discontinued her oral morphine, started with a loading bolus of 2 mg of hydromorphone, a hydromorphone drip of 1mg/hr, and added boluses of 1 to 2 mg of hydromorphone every 2 hours as needed.

Patients with neuropathic pain will be harder to control. Josh, discussed earlier in this chapter, was rotated to methadone at home to good effect. But patients with severe pain crises or whom you cannot monitor carefully at home will need admission. If you are rotating opioids because of neurotoxicity, consider adding a ketamine infusion to control the pain with fewer opioid boluses (Moryl et al. 2008). When ketamine is not an option, consider dexmedetomidine (Precedex). Anesthesia pain and palliative care specialists can be consulted to help you manage these complex patients.

Dexmedetomidine is an alpha-2-adrenergic agonist that is usually used in the ICU or perioperative settings. It produces pain relief and sedation without inducing respiratory depression, but it can induce hypotension and bradycardia (Roberts et al. 2011). The patient in the case report cited was successfully treated

in a palliative care unit, not an ICU setting, using the drug as a bridge to an interventional procedure that completely relieved her pain.

This patient had pain from a retroperitoneal mass from adenocarcinoma of unknown primary. The pain had not responded to sustained-release oxycodone, a hydromorphone PCA, oral ketamine, or intravenous lidocaine. An intrathecal pump infusing Duramorph and bupivacaine along with oral methadone had been effective for several weeks, but the patient was admitted with escalating pain from progressive growth of the mass (the pump was checked and was functioning properly, and the catheter was in place).

Reinstitution of a hydromorphone PCA led to recurrent myoclonus, so it was discontinued and a dexmedetomidine infusion was added to her home doses of methadone, with hydromorphone boluses as needed. Within 3 hours, her pain was brought under control by titrating the dexmedetomidine drip, without sedation or other adverse effects. She was comfortable until an epidural catheter/port was inserted at a new site that eliminated the pain, and she was discharged home. Had dexmedetomidine not been available, only palliative sedation to unconsciousness could have relieved her pain.

Summary

As clinicians, we strive to help even our sickest patients accomplish the goals they have set for themselves. To succeed, we must relieve uncontrolled pain. The pharmacologic agents and other treatment modalities discussed in this chapter, along with the nonpharmacologic techniques reviewed in Chapter 7, enable us to control the pain of 90 percent or more of our patients with cancer and minimize the associated side effects. Our patients will not ask us to relieve their suffering by helping them to kill themselves; instead, when they have accomplished their final tasks, they will—despite the urgings of the poet Dylan Thomas to the contrary—"go gentle into that good night."

Tables

Tables 6.1 to 6.14 follow on pages 317–329.

Table 6.1 Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Chemical Class	*Generic Name*	*Interval*	*Initial Dose (mg)*[1]	*Max. 24-hr Dose (mg)*
p-Aminophenol salicylates	Acetaminophen[2]	q4–6h	650	3000
	Aspirin[2,3]	q4–6h	650	4000
	Salsalate	q8–12h	750–1000	3000
	Diflunisol	q12h	500	1500
Propionic acid derivatives	Ibuprofen	q4–6h	400	2400
	Fenoprofen	q4–6h	200	2400
	Ketoprofen[2]	q6–8h	25	225
	Naproxen[2,3]	q6–8h	250	1000
	Oxaprozin	q12–24h	600	1200
Acetic acid derivatives	Indomethacin[2,3]	q8–12h	25	150
	Tolmetin	q8h	400	1800
	Diclofenac[2]	q8h	50	150
	Sulindac	q12h	150	400
	Ketorolac	q6h	30–60 IV load, 15–30 IV q6h	150 mg day 1, 120 mg days 2–7
COX-2 "selective"[4]	Etodolac	q8–12h	200–400	1200
	Nabumetone	q12–24h	1000 / 24 hr	1500
	Celecoxib	q12–24h	100–200	400

Sources: Modified with permission from N. Coyle, N. Cherny, and R. K. Portenoy, Pharmacologic management in cancer pain, in *Cancer Pain Management*, 2nd ed, D. B. McGuire, C. H. Yarbro, B. R. Ferell (eds), Boston: Jones and Bartlett, 1995; C. Miaskowski, J. Cleary, R. Burney, et al., *Guideline for the Management of Cancer Pain in Adults and Children*, APS Clinical Practice Guidelines Series, No. 3. Glenview, Ill.: American Pain Society, 2005. www.ampainsoc.org.

[1]In the elderly and in patients with renal insufficiency, start at one-half to two-thirds of these doses.

[2]Bioavailable p.r. via custom-made suppository or microenema (Davis et al. 2002).

[3]Available in suppository form.

[4]Rofecoxib (Vioxx), withdrawn in September 2004; valdecoxib (Bextra) withdrawn in April 2005.

Table 6.2 Cost Comparison for Equianalgesic Doses of Opioids

Drug	*Dose*	*Comparative Cost, One-Month Supply*[1]
MORPHINE		
Generic MSIR	45 mg q4h: 15 mg tabs (#540)	++
MS Contin	150 mg q12h (#60)	++
Kadian	150 mg q12h (#60)	+++
Avinza	300 mg q24h (#30)	+++
Morphine extended release (generic)	150 mg q12h (#60)	+
OXYCODONE		
Oxycodone	30 mg q4h (#180)	+
OxyContin	100 mg q12h: 80 mg tabs (#60) plus 20 mg tabs (#60)	+++
HYDROMORPHONE		
Hydromorphone IR	12 mg q4h: 4 mg tabs (#540)	+++
Exalgo	76 mg q24h: 32mg (#60) plus 12 mg (#30)	++++
FENTANYL		
Duragesic	150 mcg/hr: 100 mcg (#10) plus 50 mcg (#10)	+++
Fentanyl Patch (generic)	150 mcg/hr: 100 mcg (#10) plus 50 mcg (#10)	+++
BUPRENORPHINE		
Butrans	n/a (equivalent dose is 100 mcg/hr; this dose exceeds that allowed by the FDA)	*[20 mcg/hr = $500; if allowed, equivalent dose would cost $10,625]*
OXYMORPHONE		
Opana ER	50 mg q 12 hours: 40mg tabs (#60) plus 10 mg tabs (#60)	+++
Oxymorphone ER (generic)	50 mg q 12 hours: 40mg tabs (#60) plus 10 mg tabs (#60)	++
Opana IR	15 mg q 4h: 5mg tabs (#540)	++++
Oxymorphone IR (generic)	15 mg q 4h: 5mg tabs (#540)	++++
METHADONE		
Methadone	10 mg q8h (#90)	+ (~$12)

Source: Bridget Fowler Scullion, Pharm D, Chief Palliative Care pharmacist, DFCI
[1]Cost: + = less than $100; ++ = $101 to $1000; +++ = $1001 to $2000; ++++ $2001 to $4000

Table 6.3 Commonly Used Step 2 Opioids: Preparations Available

Name	*Initial Dose (mg), Oral*[1]	*Dose Interval (hr)*	*Dose Adjustments Needed*	*Preparations Available*[2]
Hydrocodone	10	3–4	None	IR, comb
Codeine	60	3–4	Severe hepatic or renal failure	IR, comb, IM, SQ, p.r.
Oxycodone[3]	5–10	3–4	Severe hepatic or renal failure	Comb, p.r.
Tapentadol	50	6	Moderate hepatic failure; severe renal failure	IR, ER
Tramadol	50	6	Cirrhosis or renal failure	IR, p.r., comb

Sources: C. Miaskowski, J. Cleary, R. Burney, et al., *Guideline for the Management of Cancer Pain in Adults and Children*, APS Clinical Practice Guidelines Series, No. 3. Glenview Ill.: American Pain Society, 2005. www.ampainsoc.org; H. Knotkova, P. G. Fine, R. K. Portenoy, Opioid rotation: the science and the limitations of the equianalgesic dose table, *J Pain Symptom Manage* 38:426–439, 2009.

[1]For patients weighing over 110 pounds who have moderate to severe pain.

[2]Preparations: IR = oral, immediate-release; comb = oral combination preparation with an NSAID (acetaminophen, aspirin, ibuprofen, etc.); IM = parenteral—suitable for intramuscular use; SQ = subcutaneous; p.r. = per rectum via commercial or custom-made suppository or microenema (Davis et al. 2002).

[3]See also Table 6.4 for oxycodone not in a combination preparation; that is, IR, sustained-release (SR), liquid (liq), or liquid concentrate (liq conc) oxycodone.

Table 6.4 Commonly Used Step 3 Opioids: Preparations Available

Name	*Initial Dose (mg)*[1]		*Dose Interval (hr)*	*Dose Adjustments Needed*	*Preparations Available*[2]
	Oral	*IM/IV*			
Morphine	15–30	10	3–4	Renal failure	IV/SQ, IR, p.r., liq, liq conc
Morphine SR	15–30	n/a	8–12	Renal / hepatic failure	SR, p.r.
Morphine SR	30	n/a	24	Renal / hepatic failure	SR
Hydromorphone	4–8	0.75–1.5	4	Hepatic failure	IV/SQ, IR, p.r.
Hydromorphone SR[3] (Exalgo)	12	n/a	24	Hepatic failure	SR
Oxycodone	10	n/a	3–4	Renal failure	IR, liq, liq conc, p.r.
Oxycodone SR (Oxycontin)	10	n/a	8–12	Renal / hepatic failure	SR
Fentanyl[3]	n/a	25 µg/hr	72	Hepatic failure	Transdermal
Fentanyl	200 µg	n/a	2		Transmucosal
Methadone	5	2.5	6–8	Hepatic failure	IV/SQ, IR, liq, p.r.
Oxymorphone (Opana)	10	1	4–6	Hepatic failure	IV/SQ, p.r.
Oxymorphone SR (OpanaER)	5	1	12	Hepatic failure	p.o.
Levorphanol	2	1	4–6	Renal failure	IV/SQ
Demerol[4]	N/R	N/R	N/R	Renal failure	IV, IR

Sources: C. Miaskowski, J. Cleary, R. Burney, et al., *Guideline for the Management of Cancer Pain in Adults and Children*, APS Clinical Practice Guidelines Series, No. 3. Glenview Ill.: American Pain Society, 2005. www.ampainsoc.org; H. Knotkova, P. G. Fine, R. K. Portenoy, Opioid rotation: the science and the limitations of the equianalgesic dose table, *J Pain Symptom Manage* 38:426–439, 2009.

[1]For patients weighing over 110 pounds who have moderate to severe pain. These are suggested *initial* doses. For *equianalgesic* doses, see Table 6.5.

[2]Preparations: p.r. = per rectum via commercial or custom-made suppository or microenema (Davis et al. 2002); IV= parenteral—suitable for intravenous use; SQ = subcutaneous; IR = oral, immediate-release; SR = oral, sustained-release; liq = liquid; liq conc = concentrated liquid solution; N/R = not recommended.

[3]Use as an initial dose only if the patient is already taking the equivalent of oral morphine.

[4]Not recommended for use other than for a limited time (see text).

Table 6.5 Commonly Used Opioids: Equianalgesic Doses

Drug	*Oral / Rectal Dose*	*Parenteral Dose*
Morphine	20–30 mg	7–10 mg
Hydromorphone	7.5 mg	1.5 mg
Oxycodone[1]	15–20 mg	n/a
Methadone[2]	n/a	n/a
Levorphanol	4 mg	2 mg
Oxymorphone	15 mg	1 mg
Meperidine[3]	300 mg	75
Transdermal buprenorphine	5–10 mcg/hr	
Transdermal fentanyl	12.5 mcg/hr	12.5 mcg/hr
Transmucosal fentanyl	800 mcg	n/a

Conversion from fentanyl transdermal patch to parenteral or oral morphine

	Morphine (mg / 24 hr)	
Fentanyl (μg/hr)	*p.o.*	*IM/IV*
25	50	17
50	100	33
75	150	50
100	200	67
125	250	83
150	300	100

Source: Knotkova H, Fine PG, Portenoy RK. Opioid rotation: the science and the limitations of the equianalgesic dose table. *J Pain Symptom Manage* 2009;38:426–39

[1]Rectal oxycodone is about 1/3 more potent than oral oxycodone because of less first pass effect.

[2]For dosing of methadone, see discussion in text and Practice Points box.

[3]Not recommended for cancer patients (see text).

Table 6.6 Laxatives to Prevent and Treat Opioid-Induced Constipation Syndromes

Drug	*Mechanism*	*Initial Dosage*
GENERAL		
Senna	Myenteric plexus stimulant	2 p.o. b.i.d.
Senokot-S	Senna + stool-hydrating agent	2 p.o. b.i.d.
Bisacodyl (Dulcolax)	Myenteric plexus stimulant	2 p.o. h.s.
Milk of Magnesia (MOM)	Osmotic	30–60 ml p.o. t.i.d.
Lactulose	Osmotic	15–30 ml p.o. h.s.
Polyethylene glycol	Osmotic	17 g in 4 oz water p.o. daily
MOM + mineral oil	Osmotic	30–60 ml MOM + 15–30 ml mineral oil q.d. or b.i.d.
OPIOID BOWEL SYNDROME		
Metoclopramide (Reglan)	Vagal stimulant	5–10 mg p.o. q.i.d. to 20 mg p.o. q.i.d.; or 1–3 mg/hr IV
Clonidine	Withdrawal preventive	0.1–0.3 mg transdermal patch
Methylnaltrexone	Antagonist to opioid binding to gut opiate receptors	Weight-based subcutaneous injection

Table 6.7 Antiemetics

Etiology of Nausea	*Drug*	*Dose*
Initiation of opioid therapy	Prochlorperazine (Compazine)	10 mg p.o. t.i.d. to q.i.d. or 25 mg p.r. b.i.d.
	Ondansetron (Zofran)	1 to 8 mg p.o. t.i.d.
Stimulation of chemoreceptor trigger zone	Haloperidol (Haldol)	1–2 mg p.o. b.i.d. to q.i.d., 0.5–1 mg IV b.i.d. to q.i.d.
	Prochlorperazine (Compazine)	10 mg p.o. t.i.d. to q.i.d. or 25 mg p.r. b.i.d.
Delayed gastric emptying	Metoclopramide (Reglan)	10–20 mg b.i.d. to q.i.d. or 1–3 mg/hr IV
Vertigo	Scopolamine (Transderm Scōp)	1 patch q72h
	Meclizine (Bonine, Antivert)	25 mg t.i.d. p.o.
Unclear	Ondansetron (Zofran)	4–8 mg p.o. b.i.d. to t.i.d.
	Olanzapine (Zyprexa, Zydis)	2.5–5 mg p.o. / SL qhs to b.i.d. (Zydis dissolvable wafer: 5 mg dose form only)
	Lorazepam (Ativan)	0.5–1 mg p.o. / SL/IV q4h
	Dexamethasone	2–4 mg p.o. / IV b.i.d.
	Mirtazapine (Remeron)	7.5–15 mg p.o. at bedtime

Note: For nausea, initial steps should be (1) treat cause, if identified; (2) consider changing to a different opioid agent (see text); and (3) use adjuvants to decrease opioid dose (see Opioid Bowel Syndrome in Table 6.6). SL = sublingual dissolving tablets/wafers.

Table 6.8 Psychostimulants

Drug	*Initial Dose*
Methylphenidate (Ritalin)	2.5–5 mg p.o. every morning; may repeat at noon if needed
Dextroamphetamine (Dexedrine)	2.5–5 mg p.o. every morning; may repeat at noon if needed
Modafinil (Provigil)	200 mg p.o. every morning; can increase to 400 mg/day

Note: For sedation, initial steps should be (1) treat cause, if identified; (2) use SR and IR preparations effectively; (3) discontinue other sedating agents (see text); (4) use adjuvants to decrease opioid dose (see Opioid Bowel Syndrome in Table 6.6); and (5) consider referring appropriate patients to anesthesia pain specialists.

Table 6.9 Treatment of Delirium

Drug	*Dose*	*Comments*
Typical and atypical antipsychotics		
Haloperidol (Haldol)	1–4 mg p.o. or 0.5–2 mg IV SQ h.s. or b.i.d. to t.i.d.	Can add the same dose q4h p.r.n. Do not exceed 20 mg in 24 hr. Maintain the patient on the effective dose (divided into a b.i.d. dose) for 3–4 days, then taper over 1 week, as tolerated.
Olanzapine (Zyprexa, Zydis)	2.5–5 mg p.o. / SL h.s. to b.i.d.	Can add 2.5 mg q4h p.r.n.
Aripiprazole (Abilify)	5 mg p.o. daily	Do not exceed 30 mg; does not prolong and may shorten QTc.
Chlorpromazine (Thorazine)	25–100 mg p.o., IV or p.r., b.i.d. to q.i.d.	May cause significant hypotension.
Benzodiazepines		
Lorazepam[1] (Ativan)	0.5–1 mg p.o. / SL q1-2h	Add to antipsychotic for patients with an agitated delirium. Tablets can be used p.r. for terminal delirium.
Diazepam[1] (Valium)	5–10 mg p.o. b.i.d.	Useful p.r. for patients unable to take oral medication.
Clonazepam[1] (Klonopin)	0.5–5 mg p.o. / SL t.i.d.	Tablets have been used p.r. for terminal delirium. Do not exceed 20 mg / 24 hr.
Midazolam[1] (Versed)	30–100 mg IV / SQ over 24 hr	IV drip or SQ infusion for terminal delirium.

Note: In delirious patients, attempt first to identify the underlying cause and begin to correct it as you give the agents listed. Make the patient's surroundings as familiar as possible. Ask a family member or friend to sit with the patient.
SL = sublingual dissolving tablets/wafers.
[1]*Caution*: Any benzodiazepine may exacerbate delirium, especially in older adults (>70).

Table 6.10 Adjuvants for Neuropathic Pain

Class/Drug	*Dose*	*Comments*
Corticosteroid		
Dexamethasone	10–100 mg bolus; 6 mg p.o. / IV q.i.d.; taper as tolerated	Spinal cord compression.
	4–6 mg b.i.d. to q.i.d.	Other neuropathic pain.
Anticonvulsants		
Gabapentin (Neurontin)	900–3600 mg/day p.o.	Initial dose: 100 mg b.i.d. to t.i.d.; increase by 100 mg q3d; first line for diabetic neuropathy.
Pregabalin (Lyrica)	150–600 mg/day p.o.	Initial dose: 50–75 mg b.i.d. to t.i.d.; increase by 100–150 mg q3d; first line for diabetic neuropathy.
Phenytoin (Dilantin)	1000 mg load; 200–300 mg/day	Cannot be given IM.
Carbamazepine (Tegretol)	200 mg p.o. h.s., increase q3d	Suspension available for rectal administration. Do not exceed 1200 mg / 24 hr.
Lamotrigine (Lamictal)	100–200 mg/day p.o.	Initial dose 25 mg/day p.o.; increase by 25 mg / day q2wk.
Topiramate (Topamax)	200–400 mg/day p.o.	Initial dose 25–50 mg/day p.o.; increase 25–50 mg / day q wk.
Oxcarbazepine (Trileptal)	2400 mg/day p.o.	Initial dose 300 mg p.o. b.i.d.; increase by 300 mg q3d.
Levetiracetam (Keppra)	3000 mg/day p.o.	Initial dose 500 mg p.o. q12h; increase by 1000 mg / day q2wk.
Serotonin norepinephrine reuptake inhibitors (SNRIs)		
Venlafaxine (Effexor)	150–225 mg/day	Ameliorates oxaliplatin-induced neuropathy; first line for diabetic neuropathy.
Duloxetine (Cymbalta)	60–120 mg/day	Ameliorates oxaliplatin- and taxane-induced neuropathies; first line for diabetic neuropathy.
Tricyclic antidepressants		
Amitriptyline (Elavil); imipramine (Tofranil); doxepin (Sinequan); clomipramine (Anafranil); doxepin (Sinequan); desipramine (Norpramin); nortriptyline (Pamelor)	Begin at 10–25 mg p.o. h.s.; increase to therapeutic dose (50–150 mg in divided doses)	Side effects: anticholinergic, sedation, cardiac arrhythmias, orthostatic hypotension. May need 150 mg for therapeutic effect. Amitriptyline most sedating; Desipramine least sedating, minimal cardiotoxicity; nortriptyline: least orthostatic hypotension; minimal sedation.

(continued)

Table 6.10 Adjuvants for Neuropathic Pain *(continued)*

Class/Drug	*Dose*	*Comments*
GABA antagonist		
Baclofen (Lioresal)	5 mg t.i.d.; increase by 5 mg q3d	Used for tic douloureux–like pain or muscle spasm. Target dose: 40–80 mg / 24 hr
Alpha-2 adrenergic agonist		
Clonidine	0.1–0.3 mg patch	
Cannabinoids		
Smoked cannabis		Multiple sclerosis; peripheral neuropathy; HIV neuropathy
Tetrahydrocannabinol: cannabidiol (THC:CBD)	Spray as directed.	Advanced cancer patients on opioid therapy
NMDA antagonist		
Ketamine	0.1–0.2 mg / kg IV initial	Double dose q15min until pain is relieved; then begin drip at equivalent amount per hour. Scopolamine may be needed for increased salivation.
Anesthetic		
Lidocaine	1–3 mg / kg load IV over 20–30 min, followed by infusion of 0.5–2 mg/kg/hr (10 to 80 mg/h)	Close monitoring of vital signs and patient symptoms required. Use with caution in patients with hepatic insufficiency or heart failure.

Table 6.11 Adjuvants for Bone Pain

Drug	*Dose*	*Comments*
Bisphosphonates		
Zoledronic acid (Zometa)	4 mg IV over 15 min q4wk	Caution in renal insufficiency.
Pamidronate (Aredia)	60–90 mg IV over 2 hr, q3–4wk	
RANK-L inhibitor		
Denosumab	120 mg SQ q4wk	Often effective for weeks to a few months; can cause symptomatic hypocalcemia.
Radiopharmaceuticals		
Radium-223 chloride (Alpharadin)		Alpha particles do less "collateral" damage to marrow.
Strontium chloride-89		Induces significant cytopenias; contraindicated in hypercalcemic patients.
Samarium-153 lexidronam		Induces significant cytopenias.
Rhenium-186 HEDP		

Note: For NSAIDs and corticosteroids, see text and Tables 6.1 and 6.10.

Table 6.12 Smooth Muscle Relaxants

Drug	*Dose*	*Comments*
Calcium channel blockers		
Nifedipine	10–20 mg p.o. t.i.d.	May cause hypotension, leg edema.
Gabapentin (Neurontin)	900–3600 mg/day p.o.	Initial dose: 100 mg b.i.d. to t.i.d.; increase by 100 mg q3d.
Pregabalin (Lyrica)	150–600 mg/day p.o.	Initial dose: 50–75 mg b.i.d. to t.i.d.; increase by 100–150 mg q3d.
Nitroglycerin tablets	1 tablet SL daily to q.i.d. p.r.n.	Esophageal spasm; may cause hypotension.
Anticholinergic		
Dicyclomine (e.g. Bentyl)	10–20 mg p.o. daily to t.i.d.	Mild anticholinergic side effects.
Local therapy		
Belladona & Opium (B&O) suppositories	30 to 60 mg suppository daily to q.i.d.	Pretreatment with lidocaine cream (e.g. Anusol) helps patients tolerate suppository.

Table 6.13 Topical and Oral Anesthetics

Drug	*Preparation*	*Comments*
ELA-Max	Cream (lidocaine 4%)	For procedure-related pain.
EMLA	Cream (lidocaine 2.5% + prilocaine 2.5%)	For procedure-related pain; may help in post-herpetic neuralgia.
Lidocaine	Ointment (5%, 10%), gel (5%), patch (5%)	Post-herpetic neuralgia; peripheral sensory neuropathy.
Capsaicin	Cream (0.025%, 0.075%); adhesive skin patch (0.025%)	Bone pain; post-herpetic neuralgia. Avoid heat to areas where cream is used.
Mexiletine (Mexitil)	Pill	Initial dose: 150 mg qd; do not exceed 300 mg t.i.d.

Table 6.14 Pain Behaviors in Elderly Patients Who Are Cognitively Impaired

Facial expressions	*Changes in interpersonal reactions*
Slight frown; sad, frightened face	Aggressive, combative, resisting care
Grimacing, wrinkled forehead, closed or tightened eyes	Decreased social interactions
Any distorted expression	Socially inappropriate, disruptive
Rapid blinking	Withdrawn
Verbalizations, vocalizations	*Changes in activity patterns or routines*
Sighing, moaning, groaning	Refusing food, appetite changes
Grunting, chanting, calling out	Increase in rest periods
Noisy breathing	Sleep, rest pattern changes
Asking for help	Sudden cessation of common routines
Verbally abusive	Increased wandering
Body movements	*Mental status changes*
Rigid, tense body posture, guarding	Crying or tears
Fidgeting	Increased confusion
Increased pacing, rocking	Irritability or distress
Restricted movement	
Gait or mobility changes	

Source: Table 3 in AGS Panel on Persistent Pain in Older Persons, The management of persistent pain in older persons, *Journal of the American Geriatrics Society*, 50:S205–S224, 2002. Blackwell Publishers; reprinted with permission.
Note: Some patients demonstrate little or no specific behavior associated with severe pain.

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CHAPTER 7

Nonpharmacologic Strategies for Pain and Symptom Management

Alternative Medical Systems
- Acupuncture, Acupressure, and Auriculotherapy
- Yoga

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Summary

Bibliography

Although nonpharmacologic techniques do not replace drug therapies, they are valuable adjuncts and should be incorporated into pain and symptom management strategies. These techniques, though generally "low tech," involve skilled practitioners: acupuncturists; yoga teachers; therapists skilled in massage or physical, occupational, speech, music, or art therapies; social workers, psychiatrists, and psychologists skilled in the other cognitive therapies; and spiritual counselors. Because many of the techniques can be performed by

properly trained laypersons, the practitioner often serves as both therapist and teacher, instructing patients or family members in how they can perform techniques by themselves.

Complementary and Alternative Medicines (CAMs) are used by 50 percent to 83 percent of the adult, white, English-speaking cancer patients in studies (Richardson et al. 2000; Davis et al. 2012), but you may be unaware of your patient's use of CAMs. In a 1997 telephone survey of 2055 adult Americans, 42 percent said they used at least one CAM, 46 percent had visited a CAM practitioner, but only 39 percent had told their physicians (Eisenberg et al. 1998). Twenty percent to 77 percent of cancer patients using CAMs did not tell their oncologists (Davis et al. 2012). The reasons included the patients' worries that the oncologist would disapprove, their feelings that CAM use wasn't relevant to their care, or simply that their oncologist didn't ask. Patients who do tell their oncologists, however, are more satisfied with their physicians.

Clinicians who select appropriate nonpharmacologic therapies as adjuncts can open an important line of communication with patients who are either using or considering using these treatments. At a minimum, your patients will be much more likely to tell you which of these CAM agents or practices they have adopted.

The National Center for Complementary and Alternative Medicine has defined five domains of CAM therapies. The domains are (1) alternative medical systems, (2) manipulative and body-based methods, (3) mind-body interventions, (4) biologically based therapies, and (5) energy therapies. Alternative medical systems include philosophies and practices that are completely independent of the usual medical approach. Homeopathic, naturopathic, Ayurvedic, and Native American medicine are examples of *alternative medical systems*. *Manipulative and body-based* methods include chiropractic, osteopathy, and massage. Among the *mind-body* interventions are education, cognitive and behavioral interventions, and art and music therapy. *Biologically based* treatments include special diets, such as the Atkins or Ornish diets; herbal treatments; megadose vitamin therapy; or use of particular substances not proven effective by conventional medical studies, such as laetrile. *Energy therapies* focus on energy fields within the body (biofield therapies) or outside the body (electromagnetic fields). Qi gong, Therapeutic Touch, Reiki, and healing touch are examples of these therapies.

In this chapter, I review the nonpharmacologic techniques that have the most evidence supporting their effectiveness in relieving pain and other sources of distress in cancer patients: selected alternative medical systems (acupuncture, acupressure, and yoga), selected manipulative and body-based methods, and mind-body interventions. Readers interested in a more comprehensive dis-

cussion of the domains not reviewed here can refer to the work of Dr. Barrie Cassileth (Cassileth 2011; Cassileth and Deng 2004).

Alternative Medical Systems

Alternative medical systems embrace a theory of what promotes health of the mind, body, and spirit; what causes illness; and how health and balance can be regained, which differs from that of standard medical practice. Traditional Chinese medicine (TCM) is "one of the oldest, continuously used systems of medicine known to mankind" (Smith and Bauer-Wu 2012). A comprehensive discussion of TCM is beyond the scope of this book, though I will review studies of one its components, acupuncture. If you are interested in a recent review describing the evidence for the efficacy of TCM in treating cancer symptoms, please consult the 2012 Smith and Bauer-Wu paper.

Acupuncture, Acupressure, and Auriculotherapy

Acupuncture is part of classic Chinese medicine in which, as described by Helms,*

> The language . . . reflects nature and agrarian village metaphors and describes a philosophy of man functioning harmoniously within an orderly universe. The models of health, disease, and treatment are presented in terms of patients' harmony or disharmony within this larger order, and involve their responses to external extremes of wind, heat, damp, dryness, and cold, as well as to internal extremes of anger, excitement, worry, sadness, and fear. Illnesses likewise are described and defined poetically, by divisions of the yin and yang polar opposites (interior or exterior, cold or hot, deficient or excessive), by descriptors attached to elemental qualities (wood, fire, earth, metal, and water), and by the functional influences traditionally associated with each of the internal organs.
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> Acupuncture anatomy is a multilayered, interconnecting network of channels that establishes an interface between an individual's internal and external environments, permitting energy to move through the muscles and the various organs.

*From Joseph M. Helms, An overview of medical acupuncture, www.medicalacupuncture.org/acu_info/articles.html (accessed 9/23/2102) , modified from a chapter in *Essentials of Complementary and Alternative Medicine,* Jonas WB, Levin JS (eds), Baltimore: Lippincott Williams & Wilkins, 1999; used with permission from Dr. Helms.

In acupuncture, needles are inserted beneath the skin to stimulate peripheral nerves to provide pain relief. Practitioners use their knowledge of acupuncture meridian points, extra-meridian odd points, and new points to choose the appropriate areas of the skin to stimulate, either mechanically or electrically. Acupuncture alters the pain experiences of healthy volunteers tested in a variety of pain-inducing experiments (e.g., tooth pain). In general, from fifteen to forty minutes after stimulation, pain relief becomes apparent and often lasts for up to several days. Unfortunately, less information is available about its use in cancer patients.

It is known that pain relief through acupuncture requires peripheral nerve stimulation, because anesthetizing the skin into which the acupuncture needle is inserted abolishes the effect. The spinal cord is also involved in a segmental, bilateral fashion, as was demonstrated by experiments with patients who were hemiplegic or paraplegic.

The delay in the onset of pain relief after stimulation suggests that inhibitory signals descending from the central nervous system are mediating the pain relief. The patient's hypnotic susceptibility may also be a factor—those who are not at all susceptible to hypnosis do not get pain relief from acupuncture. Release of endogenous endorphins, metenkephalin, dynorphins, serotonin, and oxytocin may contribute as well (Filshie and Thompson 2010).

It is difficult to comment on the efficacy of *real* versus *sham* acupuncture (in which the needles do not pierce the skin) because of the nature of the currently available studies. The existence of extra-meridian and new points makes choosing placebo sites difficult. In addition, there is no consensus on the ideal design for the sham intervention (Zhang et al. 2013). This does not mean that acupuncture is ineffective, just that its efficacy has not yet been definitively demonstrated.

Dr. Weiger and her colleagues, and Smith and Bauer-Wu reviewed the evidence from randomized, controlled trials that looked at the use of acupuncture. The evidence supports the use of acupuncture and electro-acupuncture for acute chemotherapy-related nausea and vomiting (Weiger et al. 2002; Ezzo et al. 2006; Smith and Bauer-Wu 2012; Garcia et al. 2013), but not for that induced by abdominal pelvic radiation.

The studies on acupuncture for cancer pain have had structural flaws, and the results are mixed. The *Cochrane Review* in 2011 (Paley et al. 2011) and a systematic review in 2013 (Garcia et al. 2013) found the data insufficient for recommending it for cancer-related pain, although Weiger felt it could be recommended.

Acupuncture used in patients with breast cancer and prostate cancer is effective for dyspnea due to bronchospasm or chronic obstructive pulmonary

disease (Cassileth and Deng 2004); it also reduces treatment-related hot flashes (Smith and Bauer-Wu 2012), alleviates the dry mouth patients experience after being treated with radiation therapy for cancer of the head and neck (O'Sullivan and Higginson 2010), and helps relieve cancer-related fatigue in patients with breast cancer, as compared with "enhanced usual care," which included "a booklet with information about fatigue and its management" (Molassiotis et al. 2012). According to the American Academy of Medical Acupuncture, the World Health Organization lists acupuncture as effective for spasm of the esophagus and cardia, hiccups, constipation, and paralytic ileus.

Acupressure involves stimulating the same acupuncture points, but pressure is used instead of needles to relieve pain (e.g., headache, backache). Acupressure may have a role in reducing nausea associated with pregnancy, motion sickness, or surgery, but the data are conflicting. Acupressure has been found helpful for acute chemotherapy-related nausea, but not for delayed nausea or emesis (Smith and Bauer-Wu 2012).

Auriculotherapy (electrical stimulation of the outer ear), however, has not been shown in rigorously controlled trials to relieve chronic pain, either from nerve injury or from low back or musculoskeletal pain syndromes.

Yoga

Yoga is "a discipline that nurtures the union of body, mind and spirit and emphasizes that as human beings, we are part of a larger whole and not just isolated individuals. One of the underlying beliefs of yoga is that there is more right with us than wrong with us, and that despite experiences of illness or disease, we are more than our illness or disease" (Ott 2002). Of the eight major branches of yoga, hatha yoga is the most often used in the medical context. The practice of hatha yoga has been shown to have significant effects in increasing strength and flexibility, normalizing heart rate and blood pressure and depth and pace of breathing, and increasing metabolic rate. It has been shown to improve the pain of patients with osteoarthritis and carpal tunnel syndrome. Breathing using yoga techniques substantially reduces the chemoreflex response to hypoxia so that patients with congestive heart failure can improve their exercise tolerance (Raub 2002).

The practice of hatha yoga usually "includes a combination of asanas (physical postures), pranayama (breathing), chanting (working with sound), shavasana (relaxation), and meditation" (Ott 2002). Patients who are bedridden can practice yoga using specially modified asanas. In fact, the effects on anxiety,

strength, flexibility, and breathing can help bedridden patients become sufficiently reconditioned to graduate to more vigorous physical therapy. Patients who are anxious about their medical procedures or the limitations, losses, and other changes induced by their disease or its treatment can benefit greatly from yoga training and practice. They can be taught how to regain control of situations that seem out of their control, and to increase their self-esteem and their endurance.

Yoga practice for practitioners and families has similar benefits, but a full discussion is beyond the scope of this chapter. Yoga instruction may be helpful in your efforts to "be present" to your patients' suffering, which is one of the hardest things anyone ever has to do. An experienced yoga practitioner can teach you and your team many ways to use your breath to steady yourselves before, during, or after difficult clinical encounters. You can also do certain yoga postures at your desk, or while waiting for an elevator, to help decrease stress and increase energy.

Manipulative and Body-Based Methods

Manipulative and body-based methods for relief of pain and other causes of distress include various cutaneous interventions, massage and vibration, transcutaneous nerve stimulation, and positioning and exercise. All these therapies can be given in the patient's home by family members or by therapists. They can add significantly to any pharmacology-based regimen.

Cutaneous Interventions

Cutaneous interventions are of particular value when the pain is localized, when muscle tension or guarding is apparent, or when the patient is waiting for a diagnostic procedure, for treatment, or for a pain medicine to take effect. Cold and warmth are routinely used in benign orthopedic and arthritic conditions. They are also very effective for cancer pain, especially that caused by bony metastases or nerve involvement.

Cold has been noted to be particularly helpful for patients suffering from skeletal muscle spasm induced by nerve injury. It interrupts the cycle of nerve ischemia caused by muscle spasms and decreases itching and hyperesthesia. Cold also seems to help patients with inflamed joints, possibly by creating numbness, and may also decrease the release of chemical mediators of pain.

Cold wraps, gel packs, ice bags, and menthol are common ways of delivering cold. Cold massage can be done by filling a small paper cup with water,

MANIPULATIVE AND BODY-BASED METHODS

- Cutaneous interventions
- Massage and vibration
- Transcutaneous electrical nerve stimulation (TENS)
- Positioning and exercise

freezing it, and then massaging the painful area with the ice that forms in the cup. The mechanism of pain relief induced by the ice massage is thought to be "hyperstimulation analgesia" or "counter-irritation." According to this theory, a mildly painful stimulus paradoxically relieves severe pain by bombarding the spinal relay system with inconsequential messages that block the transmission of the more severe pain signal. You may have experienced the effect of counter-irritation after getting an insect bite if, rather than scratch the bite itself, you've slapped or scratched the skin an inch or so away from the bite. In most cases, the itch disappears.

Patients usually tolerate cold well, but rarely, they may develop a hypersensitivity syndrome that clinically resembles cold urticaria. Cold should not be used for analgesia in patients with peripheral vascular disease or for the rare patient with cryoglobulinemia or cold agglutinin disease.

Dry or moist heat can be delivered using a heating pad, a tub full of water, a hot water bottle, plastic wrap, or a commercial hot wrap, which maximizes patient mobility. To avoid burning the skin, sessions should not last more than twenty minutes. Dry heat can also be created by topical capsaicin creams (0.025% to 0.075%) or 0.025% capsaicin adhesive patches, as described in Chapter 6. Patients should be cautioned against using a menthol product with heat because this, too, may cause the skin to burn.

Heat is contraindicated in areas where the patient is anesthetic and in areas with inadequate vascular supply, such as an extremity in a patient with atherosclerotic or diabetic vascular insufficiency. Tissue necrosis can result from the increased metabolic demands in the heated area. Heat is also contraindicated for patients with bleeding disorders, which can be exacerbated by the increase in blood flow. Short-wave diathermy cannot be used near a metal implant, including metal-containing intrauterine devices and cardiac pacemakers, or near contact lenses, because serious burns may result.

Cold and heat can be used to prevent the incident type of breakthrough pain. Some patients find alternating the two treatments to be soothing, while

others find it most helpful to combine them with any of the imaging and relaxation techniques or the other cutaneous techniques summarized below.

Massage and Vibration

Massage, like the relaxation techniques described below, slows heart and respiratory rates, lowers blood pressure, and even lessens pain and anxiety. It can also deliver a nonverbal message of affection and support.

Massage is specifically helpful for patients with muscle spasm resulting from tension or nerve injury. It is also generally useful for anxious patients, those who are limited in their ability to communicate, or those who can benefit from the closeness such touch can offer. Some patients, however, find it too personal or see it as an invitation to more intimacy than the person giving the massage intends.

Massage can include stroking, compression, percussion, or vibration and can be done with the hands, with ice, with vibration, with aromatherapy (Wilkinson et al. 2007), or with added heat (see below). Massage should not be offered to patients with coagulation abnormalities or thrombophlebitis, whom it might harm. Nurses, physical therapists, and massage therapists can all do massage and teach caregivers of bed-bound patients the basic techniques.

Vibration, either from the hands or from an electrically powered device, is also useful for pain relief. It facilitates muscle relaxation and, possibly by counter-irritation (i.e., stimulating large-diameter fibers), may also decrease sensation in the painful area. It is indicated for the same patients who can benefit from massage, but it can also help patients with neuropathic or phantom limb pain or substitute for the TENS machine (see below). A variety of devices are available, offering a number of settings and additional heat. The patient should work with the therapist to determine the optimal setting and duration of treatment.

Dr. Weiger and her colleagues have reviewed the evidence supporting the use of massage techniques to relieve pain or other symptoms (Weiger et al. 2002). Massage, in the absence of specific contraindications, can be recommended for nausea related to autologous bone marrow transplantation, anxiety, pain, and lymphedema. Evidence for its efficacy in each of these areas comes from one or more small randomized controlled trials. Aromatherapy with massage reduced anxiety and depression for the first two weeks after the intervention, in a randomized controlled trial (Wilkinson et al. 2007).

Transcutaneous Electrical Nerve Stimulation (TENS)

Transcutaneous electrical nerve stimulation (TENS) has documented utility in several nonmalignant pain syndromes, but its effectiveness has not been demonstrated in patients with cancer pain. TENS machines are portable battery-operated stimulators that activate the large-diameter fibers of peripheral nerves, thereby diminishing transmission of the pain signal.

The machines are attached to small electrodes that are placed on the skin over the nerve that is thought to be sending the pain signal, and a special current is then applied. When low-intensity, low-frequency current is applied, the patient's original pain is replaced by a feeling of numbness or of "pins and needles." If higher-intensity, low-frequency (acupuncture-like) current is applied, muscle contraction may occur.

TENS machines are especially helpful for patients with *dermatomal* pain, such as that of post-herpetic neuralgia, fractured ribs, diabetic neuropathy, or radiculopathy due to disk disease or spinal cord compression. There have also been reports of its utility in post-mastectomy pain and phantom limb pain. It may take as long as a week of use for the maximal pain relief to be achieved, and the relief provided by the TENS machine usually lasts no more than two or three months.

TENS units cannot be used for patients who have demand pacemakers, and electrodes cannot be placed over the eye, near the carotid sinus, or over metal implants (doing so may cause short circuits). TENS should be used with caution in emotionally disturbed, intellectually disabled, or senile patients, or for patients with lymphedema, which has been reported to worsen with the use of TENS. In routine use, the most common complication, occurring in 10 percent of patients, is allergic dermatitis from the tape used to secure the electrodes. If the conducting gel is used improperly, electrical skin burns can also occur.

Properly trained and experienced physiatrists and physical therapists are key to the successful use of TENS machines. They choose the appropriate stimulator and electrodes, place the electrodes on the skin, and pick the correct electrical wave form and intensity. They also educate the patient and the family about the procedures required, as well as the potential usefulness and limitations of the machines.

Because of the difficulty of treating patients with neuropathic pain, despite the relative paucity of studies using this machine, a novel therapy that is related mechanistically to TENS therapy is also worth discussing. It involves the use of the Scrambler device, which "attempts to relieve pain by providing 'nonpain' information via cutaneous nerves to block the effect of pain information." In several uncontrolled trials of patients with pain from cancer, or from various

nonmalignant causes, Scrambler therapy reduced pain significantly, and in a small randomized controlled trial conducted at the Centre for Pain Medicine, Mario Tiengo, in Milan, Scrambler therapy was more effective than guideline-based medical therapy in reducing pain and allodynia for patients suffering from chronic pain of nonmalignant origin, including postsurgical pain, post-herpetic neuralgia, or spinal cord stenosis (Marineo et al. 2012). Use of pain medications, including opioids, anticonvulsants, and antidepressants, was markedly decreased in the Scrambler group. Results persisted at three months following therapy. Further studies of this technology are under way.

Positioning and Exercise

Physiatrists and occupational therapists should be consulted for planning the care of patients who would benefit from proper positioning and exercise. These therapists are familiar with the proper equipment (beds, wheelchairs, shower/bath–assisting devices, toilets), and they can teach positioning, range-of-motion exercises, energy-conservation techniques, and safe methods for transferring patients from beds to chairs. For patients with only one arm, the therapist can demonstrate how to dress, undress, and use assisting devices with one hand.

Positioning. Cancer patients with pain may lose the spontaneous pain-relieving movements that healthy people use to minimize tissue ischemia. To relieve their pain and minimize complications such as frozen joints, decubitus ulcers, or contractures, nurses, aides, therapists, or family members need to help patients change their position. The goal is to achieve a "loose-packed" position that minimizes stress on joints. Recommended joint flexion angles are 45° at the elbow and 30° at the hip, and the hip should also be abducted 20°. This does not need to be exact, however; patients can be helped into any position that is comfortable for them.

Custom-made cushions or pillows for beds or chairs, as well as cradles to keep bedclothes off the legs, can be very helpful. Electric beds with specially designed mattresses that distribute the patient's weight uniformly are also important. For selected patients, the physical or occupational therapist may also recommend splints, orthotics, or support devices.

Dyspnea and discomfort in the chest due to excessive secretions can be ameliorated by a combination of chest physical therapy, teaching better coughing techniques, correctly positioning the patient, and teaching ways to relax the head, neck, shoulder girdle, and thorax (see below).

Exercise. Carefully constructed exercise plans can maximize patient mobility, minimize pain, and help patients function independently for as long as pos-

sible. Exercise is especially important for patients with limited joint motion due to pain, paraparesis, or paraplegia to prevent even more loss of function. The exercise can be done with or without assistance from a therapist, aide, or trained family member. Range-of-motion exercises can be done *for* the patient by one of these caregivers.

Contractures, deformities, and pressure sores are painful conditions that can often be prevented by such exercise regimens. Canes, walkers, manual or electric wheelchairs, chairs in which the seat lifts the patient to a standing position, and other assistance devices should be used as needed to maintain as much mobility as possible.

Severe lymphedema often responds to an aggressive daily regimen of massage, compression bandages, and exercise, after which the now smaller limb can be fitted with an elastic compression stocking or glove.

Mind-Body Interventions

Pain and psychological distress are, ultimately, cognitive experiences. The neospinothalamic and paleospinothalamic pathways carry pain stimuli from the periphery to the thalamus, and from there the pain signal is transmitted to numerous cortical projections. When the cortex has been severely damaged (e.g., by prolonged hypoxia), there are reflex reactions to noxious stimuli but no experience of pain.

The cortex is also intimately involved in modifying the transmission of those ascending pain signals. It has extensive input into descending neural pathways that carry inhibitory messages via the dorsolateral funiculus to the dorsal horn entry zones in the spinal cord, where they inhibit transmission of an ascending pain stimulus. Thus, if we can change the way a patient views his disease or his pain, we may be able to lessen his suffering without eliminating the noxious stimulus (Loscalzo 1996). A recent meta-analysis of studies that investigated psychosocial interventions to decrease pain in cancer patients (e.g., educational interventions and training patients in new ways to think about their pain) confirmed their efficacy (Gorin et al. 2012). Similarly, we can use cognitive techniques to modify nausea, dyspnea, and insomnia.

Something as simple as a room with a view, for example, has been shown to diminish postoperative suffering and decrease the number of days spent in the hospital (Ulrich 1984). This was demonstrated some years ago in a study that compared the experiences of cholecystectomy patients housed in rooms with two different types of views: a view of a brick wall or of a stand of trees. The rooms were otherwise identical.

MIND-BODY INTERVENTIONS

- Education and reassurance
- Diversion of attention
- Relaxation and breathing
- Guided imagery
- Mindfulness meditation and mindfulness-based stress reduction
- Hypnosis
- Biofeedback
- Music therapy
- Art therapy
- Counseling

Those with the wall view did much worse than those with the tree view. They went home one day later, and nurses recorded four times as many negative comments about these patients (e.g., "upset and crying," "needs much encouragement"). In addition, during the second to fifth postoperative days, those with the wall view asked for significantly more analgesic doses, and the type of analgesic they took was most often an opioid. Those with the tree view most often took aspirin or acetaminophen.

What patients were looking at significantly affected their recovery. A tree view led to less pain and an earlier discharge. To produce the mental equivalent of a tree view for your cancer patients, consider referring your patients for any of the mind-body interventions described below. With these adjunctive techniques, you can sometimes eliminate several sources of distress not amenable to other therapies.

Education and Reassurance

A diagnosis of cancer carries the risk of transforming a *person* into a *patient*. Physicians who are patients are at least at home in the hospital setting and are aware of the procedures they will have to undergo during their cancer staging and treatment. Though they still experience anxiety about their prognosis and the effects of the treatment, they are at least in familiar surroundings.

People who are not physicians or health care workers enter an alien environment when they become patients, and they have no idea what to expect. They do not know what tests will be ordered, or why, or what those tests will entail. Education and reassurance can be very helpful in ameliorating their anxiety.

PRACTICE POINTS: PREPARING PATIENTS FOR PROCEDURES

- Explain which tests are planned and why they are important.
- Describe what the procedure will be like, including elements from as many senses as possible (sight, smell, sound, feeling, taste).
- If surgery is planned, rehearse the major events the patient will experience while awake.
- Anticipate and correct common misunderstandings about test results.

When, for example, you send patients for their first CT scan, MRI, or echocardiogram, one of the nurses on your staff might take a few minutes to explain the procedure to them. It is important to include as many senses as possible in the description: what the room will look and smell like, what temperature it will be, what noises the machines will make, who will be there, and what will happen during the procedure.

To describe a CT scan, the nurse might say something like,

You'll be in a hospital gown on a gurney, waiting outside in a cold hall, and then you'll be wheeled into an even colder room. You'll lie on a table under the CT scanner, and you'll have a small needle connected to plastic tubing in a vein in your arm. When they put the dye in the tubing, it will go into your bloodstream, and you're likely to feel very warm and maybe even flushed. Don't worry, that's normal and will pass. There will be plenty of people there to help you, so let them know if you have any questions. You'll be awake the whole time.

As the patient listens to this thorough description, he has a chance to rehearse the procedure in his mind and raise any questions that occur to him. Later, as he actually goes through the procedure, he will become calmer and calmer as the nurse's predictions come true. Confident in his knowledge of what is coming next, he can relax.

Similarly, rehearsing a planned surgery is helpful. In one study, two groups of patients who were to have the same surgery were given either just the usual pre-anesthesia evaluation or a rehearsal of what was planned for the next day, including how much pain they should expect and how they could deal with it (Egbert et al. 1964). The patients in the group that received the rehearsal needed less anesthesia and less pain medicine after the operation, and they went home almost three days earlier than the patients in the other group.

In addition to rehearsing planned procedures, it is often useful to anticipate the possible findings and explain these to patients. If you don't, they are

sure to come to their own, often incorrect, conclusions. Take, for example, a woman with a newly diagnosed breast cancer who has to undergo staging tests.

The Importance of Dispelling Misconceptions

Except for extensive osteoarthritis, my aunt Ruth had been healthy all her life and rarely saw a physician outside the family setting (her brother, niece, and nephew were all doctors). When she was 75, she noticed a small breast lump, and it proved to be cancerous. When I called, she told me she was scheduled for bone and CT scans to help plan her therapy. She was understandably apprehensive, but I was able to reassure her that this was all routine and that, at her age, it was likely that the cancer was still localized.

Luckily, as we were talking, I remembered her osteoarthritis, and I imagined what that would look like on a bone scan. So I said to her,

Now Auntie Ruth, I need to explain about your bone scan. The scan can't tell the difference between cancer and arthritis in a bone. It will be abnormal wherever you have a bone that is arthritic, and because you have so much arthritis, the scan is likely to light up like a Christmas tree. They will want to take an x-ray of everywhere that lights up. When that happens, remember what I told you and don't worry—it's not the cancer; it's your arthritis.

When I next called to see how she was doing, she said,

You know, it went just as you said it would. After the scan, they came in and told me I would have to have several x-rays. I was very upset because I was sure the cancer had spread everywhere. Then I remembered what you told me—that everywhere I have arthritis would be abnormal on the scan. So I calmed down right away and felt much better.

As it turned out, all the abnormalities were due to her arthritis; her other test results were also negative, and she has been in remission for ten years since her local therapy. I was able to prevent her distress by anticipating both the results of the bone scan and her reaction to them and then educating and reassuring her. She, in turn, was able to use what she had learned to deal with her initial fears.

Education can also lessen the intensity of pain, especially when a patient is misinterpreting its source. A patient of mine with lung cancer and liver metastases developed acute cholecystitis. He was usually rather stoic but now seemed extremely distressed, even between bouts of colicky pain. He had apparently decided that the jaundice he had developed meant that his disease had progressed and that he was dying. Not only was he relieved when I told him that

he had gallbladder disease, but his pain intensity dropped by a third and his distress by over a half, and he regained his usual coping skills.

Dr. Henry Beecher, an army surgeon in World War II, found that the degree of pain reported and the amount of analgesia required to alleviate pain correlated more with the setting and significance of the wound than with the extent of the injury. As an army surgeon, Dr. Beecher treated extensively wounded soldiers who had survived the assault on Anzio. He found that they requested minimal or no analgesia for their wounds (Beecher 1946). Later, in his civilian practice, he found that with injuries comparable to those sustained by the soldiers, his civilian patients required much more analgesia. For these civilians, the injuries meant disruption of their usual lives and routines, loss of income, and impaired functioning. For the soldiers, however, the injury had guaranteed a ticket home. The meaning of the pain had altered the intensity of the pain experience and changed the analgesic requirements (Beecher 1956).

Whenever possible, educate patients, even if they don't directly ask, to diminish their fear and thereby decrease the intensity of the distressing stimulus.

Diversion of Attention

Distraction is a technique that can be used to decrease the pain and distress of cancer patients undergoing diagnostic procedures. If, for example, a patient is scheduled to have a breast biopsy under local anesthesia, you might suggest that she take along a portable digital music player (such as an iPod) with headphones and listen to music or a book or lecture during the procedure. The surgeon and anesthetist usually don't mind, and the patient will be spared having to listen to the operating room chatter. Distraction techniques, including a head-mounted virtual reality device, can also help patients receiving chemotherapy (Schneider and Hood 2007).

Similarly, patients should be encouraged to find activities at home or in their community that engage their attention and therefore distract them from their pain. Music (either listening to or playing an instrument), television, the Internet, movies, card playing, visitors, crafts, or interesting scenery can all be useful distractions.

Relaxation and Breathing

Sometimes, however, the pain is too insistent for distraction to be effective, and a technique directed specifically at lowering the pain intensity is required. Relaxation and breathing techniques are designed to do just that. They can free

muscles from tension so that they hurt less. Stress decreases, and patients become more relaxed; they experience less pain and are better able to cope with any residual pain.

For patients with low levels of pain or stress, relaxation alone may be effective. For those with more intense pain, who usually require pharmacologic therapy, relaxation therapies can be effective adjuvants. The best studied of these techniques are breathing modification and progressive muscle relaxation.

You are probably most familiar with the use of breathing techniques to control the pain of childbirth (e.g., the Lamaze method), but they are also effective for patients experiencing other types of pain (see Sample Relaxation Exercise, below). Progressive muscle relaxation can be used by most patients, but because of the need to tense certain muscles before they are relaxed, it should be avoided in the minority whose lesions make the muscle-tensing maneuvers too painful. It is often a component of a hypnotic trance induction (see below), but can also be helpful in itself. The therapist (e.g., a trained nurse or psychologist) or a trained family member helps the patient learn a sequence of muscle relaxation exercises, or a sequence of muscle tensing that is followed by muscle relaxing. There are various regimens, each prescribing a different number of sessions each day. Each session can last from five to twenty minutes and can be repeated up to three times a day.

When the sequence is complete, usually the muscle tension has diminished markedly and the patient is much more comfortable. The patient's blood pressure, pulse, and respiratory rate decrease; peripheral vasodilatation increases; and concentration and susceptibility to suggestions made by the therapist increase. During the exercise, the patients are very still, remaining in the same position unless given permission to move "if needed" by the therapist; they are silent and seem oblivious to external surroundings (this is also what a person in a hypnotic trance looks like).

In short, they look relaxed, and their vital signs confirm that they are. And in this relaxed state, patients are more susceptible to suggestions made by the therapist about how to control their symptoms and how to feel better about themselves. The patients themselves report that, indeed, they feel much better in a number of ways: they feel more "in control," sleep better, are less nauseated, eat and drink more, and experience less pain and less anxiety. Comparable patients receiving the same psychological supportive therapy but not taught these techniques do not experience these benefits.

Sample relaxation exercise. For each patient interested in learning progressive relaxation, I improvise a custom-made "script." Each script includes breathing modification, progressive relaxation, imagery, and suggestions that build self-

esteem. If I have taught the patient to use images to decrease pain (see Hypnosis, below), I incorporate these into the script as well.

To create the most evocative imagery, I try to determine whether the patient has an aural, visual, or kinesthetic imagination. I also take a thorough travel history, noting which sites she liked and which she would rather avoid, and I record any allergies, fears, and phobias. I would not want to ask someone who cannot swim to imagine she is sailing, or suggest to someone who is allergic to ragweed that she's walking in a field. That would hardly be conducive to relaxation!

Before I begin the relaxation exercise, I make sure the patient is comfortably positioned, in a quiet room with subdued lighting, if possible. Then I begin talking. Here is a sample script for a patient named Susan Harrison. In the script, the number of dots in each ellipsis indicates how long I pause before saying the next word. For example, . . . is a short pause, ... a longer one. I begin by directing her breathing, and then I time my words to her inhalations and exhalations:

Susan . . . I'd like you to close your eyes . . . that's right . . . Now take a deep breath in. . . . . and out. . . . . in . . . . . and out. . . . . [I am breathing at the same rate, to model the behavior for her, taking longer with the exhalations.] *And with each breath in . . . that's right . . . and out. . . . .* [talking more slowly now] *you can begin to feel more. . . . . and more. . . . . comfortable . . . If at any time you need to move . . . to make yourself EVEN . . . MORE . . . COMFORTABLE . . . you can do that. . . . The only voice . . . you need to pay attention to . . . is mine. . . . . No other sounds . . . need disturb us. . . . And with each breath in . . . and out . . . . . you're able to LET GO . . . of more . . . and more* [said on the inhale]. . . . . *tension* [said on the exhale] *. . . more . . . and more . . . of anything . . . that might be on your mind . . . letting it* [said on the inhale] *. . . all out* [said on the exhale, in a lower-pitched voice].

Now I begin the progressive muscle relaxation, using imagery.

Maybe . . . you'll find yourself . . . on a beach in the mid-morning. . . . . or by a stream. . . . . or a small lake. . . . . You are walking along . . . at a comfortable pace . . . or lying on a soft patch of ground . . . . . The sun . . . is gently warming . . . the back of your neck. . . . . your shoulders. . . . . all the way down . . . your arms. . . . . to the tips of your fingers. . . . . feeling warm . . . and COMFORTABLE. . . . . and the warmth . . . is now spreading. . . . from the back of your neck. . . . ALL THE WAY DOWN [said in a lower voice] *your back. . . . . to the bottom of your spine . . . down the back of your legs . . . and the front . . . to the tips of your toes. . . . . the muscles of your neck . . . shoulders . . . arms . . . back . . . and legs. . . . unwinding. . . . . like*

a braid unwinds in the water. . . . . more and more comfortable. . . . . more and more loose . . . like a rag doll. . . . . free. . . . . and loose. . . . . and. . . . FINE. . . . . Notice the feel of the soft . . . warm . . . breeze against your skin. . . . . the smell of the air. . . . . the light . . . as it comes through the trees . . . or glints off the water . . . the feel of the ground under you. . . . . and the wonderfully safe. . . . comfortable. . . . . free . . . feeling of this place. . . . . YOU'RE DOING VERY, VERY WELL.

If I'm doing hypnosis work to diminish her pain, I begin that here; at the end of the work, I bring her back from this special place, gently.

And each time. . . . you sit . . . or lie down comfortably at home. . . . in a quiet . . . dark . . . private . . . space. . . . . and practice. . . . . closing your eyes. . . . . breathing in. . . . . and out. . . . . and then feeling the sun gently warm your muscles . . . ALL THE WAY DOWN. . . . . unwinding them . . . like a braid unwinds . . . in the water. . . . . it will be easier . . . and easier . . . for you to get back here . . . to your special place . . . to this wonderful . . . peaceful . . . very relaxed. . . . . feeling . . . This is something you can do for yourself . . . YOU ARE VERY GOOD AT IT . . . and it is very good for you. . . . . It is important that you take this time out of time for yourself . . . whenever you need it . . . And you can bring that feeling back with you . . . as you gently return . . . feeling very pleased . . . with how VERY well . . . you have done today . . . and you will do again . . . gently . . . safely . . . comfortably . . . back [with the pitch and volume of my voice rising to the end of the sentence, as the signal for her to come back].

My patients and I both feel relaxed and refreshed after these sessions. Given the time it takes to describe the technique, take the history, and conduct the first relaxation experience, I usually reserve thirty minutes for this initial session. Subsequent sessions usually take only fifteen minutes.

And relaxation exercises are easy for patients to practice at home. Each session can take as little as five to ten minutes, or can last thirty minutes or more—whatever the patient prefers. Many people ask me to record the session to play at home to help them practice the exercise. I ask them to be sure to let me know, after they use the recording, how I can improve it for them. They might, for example, have specific suggestions for a different "special place" they'd like me to describe during the session. A note on referring patients to specialists in relaxation techniques is included at the end of the discussion of hypnosis.

Guided Imagery

Guided imagery is a cognitive technique. Here is one definition of guided imagery: "GI involves the generation or recall of different mental images, such as perception of objects or events, and can engage mechanisms used in cognition, memory, and emotional and motor control. The images are typically visualized within a state of relaxation, possibly with a specific outcome in mind (e.g., pain relief)" (Posadzki et al. 2012). Both a 2011 systematic review of randomized trials of its effects on musculoskeletal pain (Posadzki et al. 2011) and a 2012 systematic review of randomized clinical trials of its effect in patients with nonmusculoskeletal pain found few trials (<20), and most of these were poorly conducted. A majority of acceptable trials found guided imagery to be effective, while the minority found guided imagery to be no more effective than progressive relaxation, standard care, or no treatment. Given the paucity of trials and their nature, however, no definitive conclusions can be drawn about the use of guided imagery to alleviate pain.

Mindfulness Meditation and Mindfulness-Based Stress Reduction

The three general types of meditation are concentrative, contemplative, and mindfulness. Transcendental meditation, and meditation in which the practitioner focuses on a word, mantra, or image, are concentrative. Prayer is a type of contemplative meditation. Classic examples of mindfulness meditation are the Vipassana and Soto Zen traditions. The mindfulness practitioner is paying attention to everything that is going on "right here, right now," even if this includes painful or frightening physical sensations or emotions. The patient is encouraged to "observe" these feelings and thoughts as they arise during the meditation and to separate the sensations from the emotions that are occurring. Such observation can often help the patient later reframe the meanings of the sensations so that they are less frightening or less able to provoke anxiety. During a mindfulness meditation, if memories of past events and emotions, or visions of future events, arise, they are dismissed in favor of the focus on the present. Through the concentration on present sensations and emotions, patients with cancer can learn to be still, to allow time to pass. Medications have time to take effect; patients achieve emotional distance from a troubling turn of events, regain control of themselves, and are able to make decisions more easily.

Dr. Jon Kabat-Zinn, who integrated mindfulness into his stress reduction practice, has demonstrated in seven randomized clinical trials significant health benefits for persons who maintain a routine practice of mindfulness. Medical

and premedical students can reduce their stress with routine mindfulness practice (Shapiro et al. 1998). People who participate in mindfulness meditation classes learn four types of meditation: (1) body scan meditation, (2) sitting meditation, (3) walking meditation, and (4) loving-kindness meditation, along with hatha yoga postures (Carlson 2010). Patients are given CDs or MP3 recordings and asked to practice these meditations in 45-minute sessions, six days a week. They also practice different informal meditations each week, which involve being mindful during normal daily activities.

Patients who practice mindfulness meditation generally have less pain, anxiety, depression, and fatigue (Carlson et al. 2001). In a pilot study at the Dana-Farber Cancer Institute and Brigham and Women's Hospital, patients undergoing stem cell or bone marrow transplantation who practiced mindfulness meditation showed an immediate decrease in heart rate and pain, lowered anxiety, and an increase in feelings of control (Bauer-Wu et al. 2008). Mindfulness was shown to help obese patients with musculoskeletal pain increase their self-compassion, decrease their tendency to "catastrophize" the pain sensation, and find ways to cope and function with the same degree of pain they previously could not manage (Wren et al. 2012); similar findings might be expected in cancer patients.

In a randomized study in breast cancer patients who did not have pain, patients who were trained in mindfulness-based stress reduction showed improved mood, anxiety, depression, anger, fatigue, and confusion; better emotional, physical, and social well-being as well as well-being related to their roles; and fewer menopausal symptoms at the last time tested (three months after the training) compared with women who received only standard therapy. Research in this area and in the benefits of mindfulness meditation is growing, and results of new studies may help define the role of mindfulness meditation for patients with cancer and their families.

An evidence-based review on the use of mindfulness meditation in oncology patients was written by a former colleague of mine, Mary Jane Ott, MN, MA, RNCS, a trained family therapist, Reiki master, and teacher of yoga and mindfulness-based stress reduction (Ott et al. 2006). Mary Jane used to begin our palliative care team meetings with a meditation, often starting by bringing our attention to the fact that "we have arrived." She helped us focus on the present so that we could attend to the tasks before us, and as she ended, we would often hear her urge us to be "right here, right now." For each of us, those two to five minutes brought our scattered minds to the room in which we were gathered, and when we were done, we were refreshed and focused in a way that greatly enhanced the work we needed to do.

Recently, Adrianne Vincent, also an experienced teacher of yoga and mindfulness-based stress reduction as well as a leader of Buddhist meditation retreats and a current student at the Harvard Divinity School, offers mindfulness sessions twice a week to our group. Dr. Jon Kabat-Zinn has written many useful texts, some of which are available as DVDs. We used a workbook to guide us through the introductory course (Stahl and Goldstein 2010). The response has been enthusiastic; I am confident that the work she does with us, and our own practice throughout the week, improves our well-being and what we can bring to our colleagues, our patients, and their families.

Hypnosis

Relaxation therapy is helpful in itself, but it is also used by practitioners of hypnosis as an induction into the trance state. Hypnosis is an ancient and powerful technique that has a number of medical, dental, obstetric, dermatologic, and psychiatric uses. It is particularly effective in relief of pain and other symptoms in cancer patients, and even to decrease bleeding (as Rasputin knew well).

Aesculapius and his followers used hypnosis-like techniques, as did Franz Anton Mesmer. John Elliotson and James Esdaile, British surgeons familiar with Mesmer's work, also believed that the power of the mind could be used to fight pain. Esdaile (1850) performed thousands of operations in India with hypnosis as the only analgesia, with convincing results, though when he returned to England, he was ridiculed. James Braid, a Scottish contemporary of Esdaile, mislabeled the phenomenon "hypnosis," meaning a sleeplike state, only to discover later that patients under hypnosis are not asleep.

In the second half of the nineteenth century, the French physicians Ambrose August Liébeault and Hippolyte-Marie Bernheim promoted hypnosis and introduced the concepts of suggestion and suggestibility. They considered hypnosis to be a function of normal behavior. Sigmund Freud studied with Bernheim, who was a noted neurologist, but when Freud found that he did not need trance for the work he was doing with his patients, he abandoned it.

As long ago as the 1950s, hypnosis was accredited as a safe, effective procedure in both the United States and England. During the last fifteen years, experienced practitioners have noted an increase in its use for habit control and for relief of pain of malignant and nonmalignant origin.

Hypnosis is a set of techniques through which patients can be taught to regain control over situations over which they have lost much control. They can minimize their suffering while waiting for pain or antiemetic medications to take effect and can minimize the amount of medication they need, along with

the associated side effects. Appetite may be enhanced and insomnia reduced. Patients often experience newly gained independence and power, which can help even bedridden patients achieve appreciation of their own capabilities and gain a heightened sense of self-control and self-respect.

If you are interested in being trained in hypnotic techniques, I recommend that you attend one of the monthly four-day training sessions held by the American Society of Clinical Hypnosis (www.asch.net). The society holds classes for beginning, intermediate, and advanced practitioners, and you will be able to use hypnosis as soon as you finish the initial training.

Definitions. Several terms have special meaning in a discussion of hypnosis. These include *trance, induction, self-hypnosis, heterohypnosis, suggestion, distraction, dissociation,* and *negative* and *positive hallucinations.* A hypnotic *trance* is a state of altered awareness in which communication between the patient and the hypnotist is facilitated. *Induction* is the method used to help attain the hypnotic state. The hypnotist does not induce a trance but assists the patient to experience one. If the trance is induced by the patient, it is called *self-hypnosis.* Trance induced by the hypnotist is called *heterohypnosis.* Frequently, a trancelike state is spontaneously induced by events of everyday life. An athlete who is "playing through the pain" can do so because he is in trance; trance can also occur at the theater, as when a play is so engrossing that you discover, only when the lights go on, that the seats that were empty on both sides of you are now occupied.

A *suggestion* is an idea that is presented to a patient in trance and is therefore accepted with a minimum of analysis, criticism, and resistance. *Distraction* is a diversion of attention. *Dissociation* means that the patient perceives that one part of the body or personality has been split from another, or that the body is in one location but, in some form, the person is elsewhere. A *negative hallucination* eliminates the perception of something that is objectively present. For example, if one is in a trance, a loudly flapping window shade will not be heard if the suggestion is made not to hear it. *Positive hallucinations* induce the perception of something that is not objectively present. They can be auditory, visual, or tactile. It is not hard, for example, to induce an injured child to watch a favorite program on an imaginary television while his wound is being treated. Any or all of these modes may be helpful in blocking pain perception.

Misconceptions. Despite its medical utility, there are numerous misconceptions about hypnosis. The prevalence of "hypnotists" in casino shows or on cruise ships, turning people into chickens, may account for some of these. Used for medical or dental purposes, however, hypnosis is not an entertainment but a therapeutic technique. Patients in trance are *not* asleep. Their eyes may be open, and they may be sitting comfortably or walking while in trance. No one can be

made to enter a trance unwillingly, and what occurs during the trance is entirely up to the subject. Nothing can be done that violates the individual's moral or ethical beliefs. People leave the trance state whenever they want to do so—the hypnotist cannot keep them there against their will.

PRACTICE POINTS: USING HYPNOSIS IN MANAGING THE SYMPTOMS OF CANCER PATIENTS

- Hypnosis itself is not therapy, but therapy can take place while the patient is in a trance.
- Almost everyone can experience a useful trance.
- The more motivated patients are, the more they will benefit from work in trance.
- Hypnosis helps patients suffering from insomnia, anxiety, feelings of helplessness, or feelings of loss of control.
- Patients modify the experience of distressing symptoms through imagery and metaphor.
- Patients with chronic, "meaningless" pain learn how to "put the pain away for now" and to experience only "today's" pain, not yesterday's or tomorrow's.

Hypnosis itself is not therapy, but therapy can take place while the patient is in trance. The hypnotist teaches the patient how to experience a state of trance and may give helpful suggestions while the person is in trance. The hypnotic state itself facilitates the giving and receiving of suggestions relative to specific goals.

Hypnotic susceptibility. Almost everyone can experience a useful trance. Only 5 to 10 percent of the population cannot experience trance to any degree. About 10 percent of people are so adept that they can use suggestions made during trance as their only anesthetic when they undergo surgery. Differences in degrees of suggestibility, which can be assessed, may affect what can be accomplished by hypnosis. For pain relief, however, results of controlled studies differ; some have found a correlation between degree of hypnotizability and pain relief achieved, and others have found no such correlation.

Clinically, the ability to benefit from trance depends on the degree of the patient's motivation. The patient has to want to use trance to solve a problem, such as pain. In general, creative individuals with a good work history, many friends, good family relationships, and leisure activities, who are not severely

depressed, tend to make the best subjects. Even depressed people can benefit, however, if they are well motivated.

Utility in cancer patients. Hypnosis has many uses for cancer patients. It can help treat nausea, vomiting, anorexia, sleeplessness, anxiety, and feelings of helplessness and loss of control. The "rehearsal technique" recommended above to decrease the anxiety of patients about to undergo various tests, is particularly vivid for a patient in trance and has special efficacy in helping patients deal with anticipated pain or discomfort prior to surgery, radiation, or chemotherapy.

In carefully controlled studies, hypnosis has also proved to be of significant benefit in relieving acute nonmalignant pain (e.g., dental), acute iatrogenic pain, and cancer pain. In these studies, patients who used hypnosis had significantly less pain than those who did not. More controversial, it seems, is whether hypnosis is more beneficial than other cognitive techniques that reduce pain. Most studies have shown equivalency, though in some areas, hypnosis was superior.

While in a hypnotic trance, patients can use images or metaphors to change the intensity of their pain or other symptoms. For example, you can ask the patient to visualize a car speedometer with a 0-to-100 scale. Ask her to move the indicator to the number that reflects the intensity of her distress. Next, suggest that she imagine the indicator moving to a higher number and ask if the symptom has also increased in intensity. It usually has. Then suggest that she move the indicator to a position lower than it was initially, and as she does, she will usually experience a lower intensity of the symptom. With appropriate suggestions, the diminished symptom intensity will persist when she comes out of trance.

It is important to determine which images are likely to be most compelling for a given patient. The speedometer image will be useful for people who are mechanically inclined or who just like to drive. But it may not be helpful for someone with different interests. For those who are musical, you can use the image of the volume control on a radio. For visual people, you can suggest they use a rheostat to change the symptom intensity just as they do the intensity of light in a room. Visual people also find they can change the "color" of their symptom, from a hot, painful color such as red to a cooler, more comfortable one such as blue.

If a patient has chronic pain that is not serving as a danger signal, you can help him find an old trunk in the attic in which he can "put the pain" and "check on it" whenever he feels the need. He will still react to new pains or to changes in the existing pain, which he can report to you for evaluation. Children like to go to the deck of a spaceship and search for the colored wire and matching light switch that correspond to their pain. When they find them, they turn the switch—and the pain that came with it—to "off." You can create any number of

metaphors and images once you know the patient's personality and his likes and dislikes.

You can also alter time subjectively, as you know if you've ever been to a boring lecture or an exciting sports event. Using hypnosis, you can prolong patients' pain-free periods and shorten the painful ones. And you can use patients' memories of other episodes of anesthesia, such as spinal anesthesia, to teach them to bring back that numbness to relieve their pain. They can also be taught to develop anesthesia in a glovelike distribution and to use that "anesthetized" hand to spread a feeling of numbness to painful body parts.

Distraction. Montaigne once wrote, "We feel one cut from the surgeon's scalpel more than ten blows of the sword in the heat of battle." Our peacetime warriors, the weekend football and basketball players, experience the same phenomenon—it is not until after the distraction of the game is gone that the bruises or even broken bones become apparent. Distraction, then, is a powerful modifier of the pain experience.

Without even realizing it, most of us use distraction when we need to do something that may make a patient uncomfortable. Performing a pelvic or rectal exam, for example, we engage our patient's attention by talking about something interesting. I have seen hematologists extract sternal bone marrow samples with no other anesthesia than the fascinating story they were telling—they were out of the door before the patient even realized a needle had been stuck in his chest, marrow extracted, and a Band-Aid placed on the wound.

Distraction is much more powerful, however, when the patient is in a hypnotic trance. Trance is especially likely to be effective in the emergency room, when it is spontaneously induced by both the injury and the setting. You might have a patient with a serious limb laceration, for example. Using your voice and nonverbal cues, such as a hand on the shoulder, to help induce or simply deepen the trance, you can suggest that the patient imagine that the injured limb is covered with newly fallen snow, which is lightweight and cold. You can then suggest that the coolness and comfort are spreading throughout the injured limb. This image is likely to lessen the bleeding as well. While the wound is being closed, you can ask the patient to concentrate on guessing how many stitches it will take. Engrossed in that discussion, and in trance, she will often be distracted from the associated pain. This technique is especially effective with children.

Dissociation. Bedridden patients can often use dissociation during trance to escape from their pain. They can "go" to their favorite vacation spot and retrieve enjoyable experiences while in trance, through self-hypnosis or heterohypnosis. The hypnosis practitioner doesn't even have to be there to help them; she can

make them a recording on portable digital music player (such as an iPod) filled with suggestions that enhance the patient's ability to dissociate.

Patients can also be taught during trance to dissociate a painful part of their body; they will then experience that body part as "not there" or "not theirs." The former is a negative hallucination; the latter is dissociation. A patient might, for example, dissociate the body part in anticipation of a painful procedure. Putting in an IV, for example, can be less painful if you make the suggestion that the arm is not really part of the body and that what happens to it doesn't need to affect how the patient feels.

You can further enhance patients' comfort during this procedure by helping them induce anesthesia in the arm. When they are in trance, you might suggest that they use the cool sensation created by the alcohol swab to help them recall any previous feelings of numbness they've had, and then to extend the feeling of coolness in the arm to that numb feeling; when the needle enters the skin, they will feel it, but it won't hurt. When the procedure is completed, you must suggest that the sensation will return to normal; otherwise the arm might stay numb for some time and not respond normally to a painful stimulus (e.g., extreme heat).

Making a referral for relaxation therapy or hypnosis. While you can do a great deal with the techniques outlined above, some patients will benefit from more intensive work with someone fully trained in the use of hypnosis and relaxation techniques to relieve pain. You may find, however, that patients resist such referrals. They may misinterpret your suggestion as implying that you don't really believe they are having pain. Or they may just be afraid of the techniques themselves. Preface the referral by saying something along the following lines:

The pain syndrome you are experiencing is a very complex one, but there are many effective treatments for it. Remember when you were first diagnosed with cancer and I felt that you would benefit from both surgery and radiation treatments? That probably seemed reasonable to you, since the side effects of each treatment would be minimized, and yet you would obtain the best possible result. Well, I think we also need to use a number of different treatments to relieve your pain.

In addition to taking the medications I will prescribe, I want you to learn some other techniques to lessen your pain. Two of these are hypnosis and relaxation therapy. People with the kind of pain you have can benefit a lot from these techniques. And since you won't need as much pain medicine, you'll have fewer side effects from it. Unfortunately, I am not really an expert in teaching relaxation techniques, but [the psychologist, psychiatrist, social worker, nurse] *is and would be happy to teach them to you.*

[She] *may, in fact, offer to teach you several techniques that can help you relieve your pain. When you first meet* [the practitioner, she] *will assess your pain, as I did, so that* [she] *can choose the most effective techniques to use or to teach you to use at home.* [The practitioner] *would also be happy to teach these skills to anyone in your family who is interested. Your work with* [her] *will be confidential, just as it is with me.*

You, your family, [the practitioner], *and I will continue to work together to be sure you achieve a degree of pain relief that is satisfactory to you. So I'd very much like to hear which treatments you are using and how each of them is helpful.*

Implicit in such an introduction is your belief that the patient is really in pain. You have also communicated your faith in the colleague you've recommended and in the techniques that person will suggest to ameliorate the pain.

Biofeedback

Biofeedback, in its narrowest sense, is an electronic teaching aid that helps patients monitor certain physiological functions, such as muscle tension or skin temperature, and modify them. It has been found efficacious for patients with various nonmalignant conditions, including spasmodic torticollis, spasticity, or paresis resulting from cerebrovascular accidents and urinary or fecal incontinence, as well as for the elderly. It is also effective in mild hypertension and in some patients with migraine or tension headaches, but it is no more effective than other methods of relaxation for these conditions. There are no controlled studies of its efficacy for patients with pain of other etiologies, however, including cancer pain.

Music Therapy

Introduced into palliative care in the United States and in Canada in the 1970s by Lucanne Magill, Susan Munro, and Balfour Mount, music therapy is "the creative and professionally informed use of music in a therapeutic relationship with people identified as needing physical, psychosocial, or spiritual help, or with people aspiring to experience further self-awareness, enabling increased life satisfaction" (Magill 2001, 2010; O'Callaghan 2010). Music therapy can be done with individuals or groups in the outpatient, home, or hospital setting.

Music therapy offers diversion, distraction, and enhanced relaxation. It may benefit some patients with complex pain problems, though few studies documenting its effects are available. Music therapists are specially trained individuals who involve patients in active music making, song writing, and selecting the

recorded music that is meaningful to them. Therapists trained in the Bonny method of guided imagery and music incorporate music into a program of guided imagery and relaxation aimed at helping patients gain more self-awareness and individual development. Therapists or volunteers can also assist patients in selecting tapes designed for relaxation or can make personal tapes for them.

Music therapy is particularly useful in assisting patients with life review. It takes them back into memorable times of their life through the music that was associated with those times. Patients can also work with therapists to create music-related legacies. They can put music that has been meaningful to them on a CD or on a portable digital music player (such as an iPod), rewrite the lyrics of familiar songs, or create new songs that reflect what they need to say. Observational studies indicate that patients, families, and staff have positive responses to this therapy, as long as they can choose the music or musical style. Not only were they able to remember good times, but also in many cases they felt "transported" to new, pleasant experiences (O'Callaghan 2010). A review of research issues in music therapy for adult cancer patients found many challenges in performing the research, but also evidence of improvement in pain and other physical symptoms, psychological distress, and mood (Hanser 2006).

Even in the absence of formally trained music therapists, research supports music "therapy" (i.e., listening to music through headphones) as a nursing intervention to relieve patients' pain, anxiety, nausea, or vomiting (Olofsson and Fossum 2009). Suzanne Hanser and her colleague Susan Mandel produced a very useful handbook with accompanying CD that patients and families can use to manage their pain and stress (Hanser and Mandel 2010).

Practitioners of music thanatology use music to alleviate the distress of dying patients (Horrigan 2001). Therese Schroeder-Sheker is a harpist, singer, composer, clinician, and educator who founded the field of music thanatology thirty years ago, creating both the Chalice of Repose Project and the School of Music Thanatology at St. Patrick's Hospital and Health Sciences Center in Missoula, Montana. Training in music thanatology requires five semesters plus a one-year internship.

Schroeder-Sheker recommends a polyphonic instrument to "deliver prescriptive music": a piano, organ, lute, guitar, or harp, or a keyboard that simulates these instruments. She considers the harp to be "particularly effective" in this work. Instrumentalists position themselves on either side of the patient's bed; Schroeder-Sheker always uses two harpists for the vigils she conducts. Vigils can last for an hour or more.

Before and after each session, music thanatologists assess the patient's pulse rate and strength, pattern of breathing, temperature, and any indications in the

face or movements of the body that suggest distress. The music is synchronized to the dying patient's heartbeat and respirations and can produce a profoundly calming, peaceful result. Breathing becomes deeper and easier, grimacing and muscle tremors resolve, and a deep sleep begins in patients who were unable to sleep before the session.

Schroeder-Sheker draws the parallel between childbirth and the dying process, both of which can be eased by the right partnering. Music thanatologists act as such partners. They help the patient, and they help the family and loved ones express their emotions and say good-bye (Hilliard 2001). They are "called to protect the sacredness of some events, and death is one such sacred mystery."

Art Therapy

Art therapy enables patients and families to use symbolic representations to express and explore their thoughts, hopes, and fears. Patients under active treatment, or bereaved family members (including children and adolescents), can participate. They create an art piece and then, with the help of the art therapist, reflect on its implications. Often the *process* is more important than the quality of the artwork. The making of the piece may enable the patient to express feelings that otherwise would be suppressed. Anger or frustration that cannot be directed at the physician or at God can manifest, for example, as pounding on clay; these emotions can be noted and then discussed with the art therapist. Hope, gratitude, and love can also be expressed in artistic creations when words do not come easily or do not suffice.

Art therapists are trained at a postgraduate level and certified. They can work in the outpatient setting or in homes, hospices, or hospitals. Art therapy is particularly helpful when patients or their families are having difficulty communicating verbally about their struggle with the illness and what it has meant for their lives, either because of language or cultural differences or because of unease with talking about such important issues. Physical, social, psychological, and spiritual struggles; concerns about body image; and lack of self-esteem are all areas that can be explored by art therapists. Studies supporting the benefits of art therapy suggest it can contribute to patients' sense of well-being (Reynolds et al. 2000), but more research is needed.

Spiritual Counseling

Patients and their families often benefit from both psychological and spiritual counseling. I discuss psychological counseling when I review the assessment

GOALS OF SPIRITUAL COUNSELING

- Enable patients to give and receive love, have hope, express themselves creatively, and have meaning and purpose in their lives.
- Help patients reconcile with those from whom they have been estranged.
- Eliminate feelings of guilt and shame.

and treatment of anxiety and depression in Chapter 9, so here the focus is on spiritual counseling.

A consensus conference held in 2009 to explore the role of spirituality in palliative care (Puchalski et al. 2009) came to this definition of spirituality: "The aspect of humanity that refers to the way individuals seek and express meaning and purpose and the way they experience their connectedness to the moment, to self, to others, to nature, and to the significant or sacred." Spiritual needs are involved with transcendence and may be defined as the need to give and receive love, to have hope, to be able to express ourselves creatively, and to have meaning and purpose in our lives (Highfield and Cason 1983; Jacobs 2008). We need to be reconciled with those from whom we have been estranged (Cosh 2006), and we need to resolve feelings of guilt and shame (Fitchett and Canada 2010). Spiritual counseling addresses these needs, reestablishes hope and meaning, and, for the terminally ill, enables them to resolve issues that might otherwise prevent a peaceful death.

Spiritual care is a core part of palliative and hospice care, of course, but attention to patients' spiritual needs can be an important part of the care of any patient with a potentially life-limiting illness like cancer. Patients with advanced cancer who have their spiritual concerns addressed by the medical team are more likely to enroll in hospice and, among those whose spirituality is an important source of coping, to enroll in hospice with less aggressive care at the end of life (Balboni et al. 2009). Spiritual care is also associated with a better quality of life for patients as they approach death. A large majority of black and Hispanic Americans with cancer (88 percent and 74 percent respectively) report that religion is very important to them, compared with only 44 percent of whites ($p < .001$) (Smith et al. 2008).

A diagnosis of cancer is often an occasion to reflect on past events—achievements, failures, loves won and lost—and to put everything into perspective. It is also a time when we reexamine our relationship with God, with those we love, and with those who love us. We need to be reconciled to our failures

and to bring closure to relationships left unsettled. And we look for hope, if not for a cure. We'd like to know we can accomplish those goals that remain to us and that we will die a dignified, pain-free death.

For some people, this will be a time of great creativity as they seek a way to communicate what their life has been or what they think is most important. Be it through an audio recording, a DVD, a video, a book, a scrapbook, or a painting, that work will express what they need to leave behind.

There are patients, however, who cannot find the meaning alone, who feel that they have been forsaken by God or those they love, or who see no reason to hope. They may be angry with God, or have unresolved guilt, thinking that their own sin caused their disease or its recurrence. They may feel isolated, changed by their illness into someone they don't recognize, someone whom their family and friends cannot understand or love. Their resulting emptiness, confusion, existential crisis, or despair may be very painful. Chaplains are particularly skilled in aiding patients with any of those needs (Emanuel et al. 2012), especially board-certified health care chaplains, who are trained in ministering to those of any faith tradition, including agnostics and atheists (Association of Professional Chaplains 2009).

For dying patients, spiritual tasks may take on a new urgency, becoming important to prevent despair (Emanuel et al. 2012). Palliative care teams therefore need a chaplain as their spiritual care specialist (Pulchalski et al. 2009). Chaplains perform a comprehensive spiritual assessment and search for the etiologies of patient suffering. Their approaches to what they find may include techniques from the patient's own religion or other faith traditions, the arts, or psychological counseling (Jacobs 2008). Their ethical standards prohibit them from proselytizing their own faith to patients (Puchalski et al. 2009).

Programs accredited by the Association for Clinical Pastoral Education (ACPE) train chaplains in hospitals throughout the United States. Unfortunately, it may be difficult to find a trained chaplain in your institution, since in 2009, there were only about 8,100 members of professional chaplaincy organizations in the United States (4,000 members of the Association of Professional Chaplains, 3,700 members of the National Association of Catholic Chaplains, and 400 members of the National Association of Jewish Chaplains; Puchalski et al. 2009). Therefore, even though clinicians are not professionals in this area, those caring for cancer patients are likely to benefit from developing some basic skills that will be helpful to those in spiritual pain: the ability to be with people and to listen to them rather than focusing on what we can do for them (Cosh 2006). We need to think about spending the time we would otherwise spend

retrieving and analyzing test results, conferring with consultants, and writing orders in just being with our patients with advanced cancer, especially if they are suffering. We need to listen to their spiritual questions, understanding that they don't really expect answers from us. In some patients, we may detect signs of spiritual health, as I should have in Miss Brown ("I'm all right, dear. Are you?"; see Chapter 1). In others, we may determine during the course of our listening that the patient has specific problems that could benefit from the extra time another team member could give, especially the hospice or hospital chaplain.

Some core spiritual screening questions include " 'What is your faith or belief?' 'Do you consider yourself spiritual or religious?'; 'Is it important in your life?'; 'Are you part of a spiritual or religious community?': 'How would you like me, your healthcare provider, to address these issues in your care?' " (Puchalski and Romer 2000, p. 131). The spiritual history itself can be incorporated into the social history, or highlighted, depending on what you find. I find it helpful to have a framework when I start to explore an area that is new for me, and when I began taking spiritual histories, I used a series of questions that Dr. Puchalski had refined, called the FICA tool (faith/beliefs, importance, community, address in care or action) (Puchalski and Romer 2000).

I ask patients about their faith tradition or the religion in which they were raised and what beliefs they held (F). I then ask how important (I) those beliefs are to the patient. I ask also whether they worship in a community (C) of others of similar beliefs and whether that community is important to them. I might find out, for example, that someone was raised in the Jewish religion, but that they are no longer affiliated with a temple and do not really align themselves with traditional Jewish beliefs. Or, since I work in a referral hospital, I may discover that the patient's church community is far away, and that communal worship was always an important source of support to the patient that is now missing. These questions, therefore, help me understand whether there is a spiritual issue contributing to the patient's suffering.

Finally, I ask them to let me know which aspects of their care they think were affected by their beliefs, so that I am sure to know what, if any, actions they want me to take in concert with these beliefs. For example, if washing before prayers was important to a bedridden Muslim patient, we let the unit staff know, so that they would understand why the patient needed fresh water and towels five times a day. Other spiritual assessment tools may be more congenial to you; they include HOPE (hope, organized religion / personal spirituality, effects of care and decisions), and SPIRIT (spiritual belief system, personal spirituality, integration, rituals/restrictions, implications, and terminal events) (Puchalski et al. 2009).

Do I pray with them if they ask me to? It depends. I refer you to the guidelines in the literature (Puchalski et al. 2009; Lo et al. 2003) to help you answer this question for yourself.

Hermes Listener

Paula Balber (2006), in her discussion of the "Hermes listener," suggests that a useful strategy for helping patients make meaning and thus fulfill a spiritual need is to ask questions that enable patients to develop their own myths—to go on their own hero's journey, as described by Joseph Campbell. This journey, as Campbell recounts it, begins with taking leave of the familiar after the arrival of the messenger with the bad news (that's us, giving them their diagnosis and prognosis). The hero acquires a guide and traveling companion who will take him to the second step of the journey, where he will encounter all the issues that keep him from being able to face death with a quiet mind and spirit.

Health care professionals, clergy, or family and friends can serve as this guide and protective figure (Balber 2006). And they can help as patients relate stories in which they recast moments of the past to give meaning and purpose to their lives, reconciling themselves to what has gone before, and creating their legacies.

Listening to such stories is hard work, though it may be very rewarding. In addition to standard questions such as "What was your childhood like? Tell me about your family. What did you do for a living? What do you think will happen next?" (Balber 2006), you might ask questions with a more personal focus (Betts 1988):

Do you have any objects that you cannot throw away? What were your lucky breaks? Where were your life's turning points? What is your favorite memory? How was your life different from what you expected? In what family members do you recognize yourself? What would you like to have done instead of the work that you chose? How have you coped with the deaths of ones you've loved?

These questions are likely to lead to the kinds of stories that will help patients address the issues they need to address.

In the stories, you are likely to notice metaphors for the problems that the patient is currently facing. The patient may reveal her fears, how she overcame or dealt with them in the past, and how she regained control of the situation. You can share your admiration for how she overcame each of these problems before, and in so doing, without actually mentioning current problems, you will be expressing your confidence that she will be able to deal just as well with them now.

The stories may also be vehicles in which patients can release their anger, resentment, or disappointment. With the help of the listener, the patient may be

able to understand the purpose of past painful events or reconcile with people he wants to see again before he dies. Individual stories become part of the whole tale of his life, helping the patient regain perspective and meaning.

Speech and Language Therapy

Speech and language therapy can help patients regain the ability to communicate. This therapy also enables some patients with swallowing difficulties to eat again. Speech, language, and swallowing problems affect about a quarter of patients enrolled in hospice programs (Jackson et al. 1996). It is important to refer patients early whenever problems can be expected. Patients with brain metastases, for example, who may develop cognitive decline, or patients who may lose their ability to speak postoperatively or following prolonged intubation for respiratory compromise can benefit from a therapist's training them in other communication techniques (e.g., using a communication board) well before they are actually impaired. After initial assessment, the therapist monitors changes, provides exercises to enhance audibility and clarity of speech, and teaches ways to compensate for loss of speech. The therapist can also provide clarification and education to family members, helping them cope with the changes, anticipate what is ahead, and learn how to maximize their ability to connect with the patient.

Speech and language therapists are also called in to assess and provide therapeutic suggestions for patients with difficulty swallowing due to oral and pharyngeal dysfunction. They can assess aspiration risk and suggest safer postures or positions for eating or how the food consistency can be modified to diminish the chance of aspiration. Referrals are indicated as soon as the patient or family notices frequent choking or coughing after eating, or difficulty handling normal oral secretions.

Summary

The nonpharmacologic strategies for managing pain and other sources of suffering in cancer patients add an important dimension to the treatment plan. Acupuncture can be a significant adjunct to symptom management. Yoga practice brings together mind, body, and spirit, strengthening, refreshing, and energizing them all. Patients, their families, and the treatment team can benefit from yoga practice. Many of the manipulative and body-based methods for providing relief to patients can be performed by friends and family and can be a significant source of satisfaction for these caregivers. The practice of relaxation, mind-

fulness meditation, or hypnosis, and work with a spiritual counselor, can offer a sense of control and hope, meaningfulness, and self-worth throughout the course of illness. Working with a speech and language therapist, patients can enhance both their ability to communicate and their ability to eat. These approaches, along with art and music therapy, enhance the lives of patients with cancer. The meditative techniques similarly can enhance the lives of their families and of the doctors and nurses who care for them.

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CHAPTER 8

Sexuality, Intimacy, and Cancer

with Amanda Moment, MSW, LICSW

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Next to conversations about the end of life, the hardest topic for most of us to broach with patients may be sexuality. It can feel just too intimate, with its minefield of cultural pitfalls and awkward moments. No wonder most of us would prefer to avoid it. In this chapter, Amanda Moment, MSW, LICSW, my colleague and an expert in the palliative care needs of cancer patients, helps us explore why sexuality is important, what barriers we face, what patients really want from us, and how to improve our practice, and it will be her voice that is speaking as "I."

Many studies show that patients want to know about the effect of cancer and cancer-related treatment on their sex lives, and that we clinicians are notoriously poor at helping them anticipate and navigate these concerns. This chapter includes a review of the literature about sexuality and cancer. Those of you already familiar with this information may want to skip ahead to the sections called "How to Approach the Subject" and "Practice Suggestions." Tables are on pages 418–422.

Why Is This Subject Important?

Sexuality and Quality of Life

The World Health Organization recognizes—not at all surprisingly—that sexuality and intimacy are important contributors to quality of life (2002). Sexuality can mean a variety of things depending on a person's age, gender, culture, religion, education, sexual preference, and personal history. It includes our relationship to another person, such as how we think about our ability to have sex with a partner, and it also includes a woman's sense of femininity before and after a mastectomy or a man's sense of masculinity after androgen-deprivation therapy. Our patients are each likely to have unique views of their own sexuality and

concerns about changes that treatment will bring. Often the great issues of identity, engagement in life, sexuality, and intimacy are related so that when one diminishes, so can the others (Hawkins et al. 2009; Navon and Morag 2003).

Sexuality and Cancer: Impact and Prevalence

Given the importance of sexuality and intimacy for a patient's sense of self, the changes brought about by cancer and its related treatments are significant. With more and more patients living with cancer as a chronic disease (almost 12 million), large numbers of people are moving beyond the initial goal of survival and wondering how to live as well as they can with their diseases (Howlader et al. 2011). A study by Ferrell and colleagues (1995) cautions us that unaddressed changes in sexuality can be among the most negative influences on the social well-being of a cancer survivor. And because social support is a major contributor to one's recovery from illness, a decrease in sexual contact (one form of social support) can lead to a feeling of isolation, making recovery more difficult (Weijmar Schultz and Van de Wiel 2003).

Estimates of sexual dysfunction after various cancer treatments range from 40 percent to 100 percent. According to data from Leslie Schover (1999) and the National Cancer Institute (2013), 50 percent of women who have breast or gynecological cancers and 60 to 90 percent of men who have prostate cancer (depending on therapy type) have long-term sexual dysfunction; estimates for other kinds of cancer are less well documented. Sexual problems often become more apparent or distressing during the first months after the completion of active treatment (Schover 1999). The most common problems are dyspareunia (pain with intercourse) for women, erectile dysfunction for men, and loss of desire for both men and women.

One couple, in which the husband was battling renal cancer, talked about the medical interventions that slowed and then stopped their sexual life altogether. They stated that they were both tired from balancing the many demands of the illness and that sometimes he would be in too much pain for her even to touch him. Once the treatments were over, they both found themselves avoiding a sexual reconnection. He stated that he had a hard time looking in the mirror because of all his scars, and she reported that, in a desire to be supportive, she had not wanted to push him. While they wanted to learn how to bridge the gap between them, they didn't know how to approach a conversation about these changes, and before I met with them, no one had explored this area of their lives with them. They were both very grateful that I had asked about it!

Stigma

Though we may not realize it, patients are often faced with the "dual stigmatization of cancer and sexual dysfunction" (Navon and Morag 2003). Some unaddressed sexual issues or concerns may interfere with patient compliance with treatments such as hormone therapy (Schover 1999). Unfortunately, our attitudes can contribute to this sense of stigma. MacElveen and McCorkle (1985) say that when we treat patients as asexual beings because of their age or how ill we think they may be, we can unwittingly hurt people whose sexuality is already traumatized and vulnerable. Because of the power we hold, our patients often feel they need our permission to discuss issues of sexuality and intimacy, and they are likely to be grateful for reassurances that what they are experiencing is normal (Hawkins et al. 2009).

Mrs. A was a cancer survivor who told me, *"It is amazing how quickly you become invisible to those taking care of you. Sometimes it feels like they could treat the disease without ever having to really look at you. No one ever asked me about the impact on my sexuality, and yet it was there. I didn't feel that it was acceptable to bring that up."*

Are We Talking?

Despite the importance of this issue, often neither we nor our patients have the language to even begin the discussion. As Weijmar Schultz and Van de Wiel (2003) noted, when cancer enters the picture, "suddenly, words need to be found to discuss and express wishes, desires, options, and impossibilities." The data suggest that we are missing the mark. For example, although patients want health professionals to bring up issues of sexuality and intimacy (Hordern and Currow 2003; Hughes 2000; Price 2010; Ananth et al. 2003), health care professionals believe patients will bring them up if they are important to them (Carr 2007; Saunamaki et al. 2010; Price 2010). We are more likely to talk about sexuality and intimacy with patients whose cancer or its treatment directly affects sexual function (Schover 1999; Shell 2007); even in those cases, however, the number of us who initiate this conversation is low (Hawkins et al. 2009; Hendren et al. 2005), and patients are only minimally satisfied with the information we give them (Bourgeois-Law and Lotocki 1999). One study showed that health professionals who did address sexuality with their cancer patients ignored the emotional effects and only talked about the physical implications, such as erections, menopause, and fertility (Hordern and Street 2007).

Whose Responsibility Is It?

Because of the natural power differential between us and our patients, between what they think we know and what they're sure they don't, and between a healthy person and one who is ill, it's really our responsibility to bring up the topic of sexuality, and to incorporate sexuality screens into our practice. Patients, for example, may believe that raising the subject, which is already fraught with stigmas, shame, and uncertainty, is a waste of our time. If, in addition, they sense our discomfort with this topic, they are likely to avoid bringing it up (Gochros 1986).

Some ways in which we might be sending subtle cues of our own discomfort include "breaking eye contact, changing the subject, using closed-ended questions and euphemisms" (Gochros 1986, p. 10). We need to work on making ourselves more accessible to discussions of sexuality and letting our patients know that we are. This chapter will offer some guidance.

Positive Outcomes

What can we hope for if we discuss these issues?

Mr. D, a 29-year-old single male who had been undergoing treatment for testicular cancer, said that it had been really useful for his oncologist to open up the topic of sexuality with him. He had been casually dating prior to his diagnosis but felt that he had no outlet for discussing with anyone he knew how his health and his romantic life intersected. *"I hadn't realized that this was a subject I could talk about with my doctor, but once he asked if I had any questions about how it was affecting intimacy in my life, I realized I wasn't alone with it."*

Even if patients don't have questions about sexuality or intimacy, you can try approaching your relationship with them in an open and curious manner; that lets them know that you are interested in all the ways cancer is affecting their lives and encourages them to talk with you about things that are concerning them as people, not just as patients. You can show that you're someone who provides care for the whole person rather than simply treating their cancer, which will help to decrease any sense of isolation or embarrassment arising from their sexuality. Engaging in these conversations also increases their ability to make informed decisions about their care. And providing adequate support can enhance overall patient satisfaction, making them less likely to demand inappropriate amounts of time and energy from you (Schover 1999).

How Do Cancer and Related Treatments Affect Sexuality?

According to Weijmar Schultz and Van de Wiel (2003 p. 122), "sexual problems are nearly always caused by a complex combination of physical, psychological, and social problems" and often are influenced by people's sexual functioning before they became ill. The authors add that "disease extent, magnitude of treatment, and location of disease are all important determinants of risk" (p. 122). A Macmillan Cancer Support survey offers a helpful categorization of the aspects of sexuality that change when someone becomes a cancer patient: (1) physical ability to give and receive sexual pleasure; (2) thoughts about one's body or body image; (3) feelings, including fear, sadness, anger, and joy; and (4) roles and relationships (Davis 2009). Below is broad overview that may add to your understanding about each of these aspects. A list of the changes that affect sexuality is found at the end of this chapter (Table 8.1).

Physical Changes

Much of the information below is a highly condensed version of sexuality information available at the National Cancer Institute's website, with specific articles listed at the end of this chapter, under Resources.

Sense of Self and Emotional Changes

Mrs. B. was a 56-year-old woman with ovarian cancer who had an ileostomy, colostomy, and a venting g-tube due to cancer-related complications. One day she confided in me that she didn't want to see herself naked anymore. The landscape of her body and self-concept had changed so much that it no longer felt like her own. She echoed a theme I often hear from patients about feeling as though they have been betrayed by their bodies and are unable to feel at home in them.

Disruption of sexual identity is only one of the changes cancer and its treatment can bring. Others include emotional disturbances, general malaise, apathy, and loss of self-confidence (Weijmar Schultz and Van de Wiel 2003), as well as broader feelings of asexuality or undesirability (Navon and Morag 2003). Patients often bring up feelings of uncertainty about who they are now and report a surreal sense of being out-of-body. Those whose ability to have sexual intercourse has decreased may mourn this loss and experience feelings of self-blame, rejection, lack of fulfillment, frustration, and obligation (Hawkins et al. 2009).

Social and Interpersonal Changes

Experiencing cancer can affect peoples' desire and ability to interact with their world. Patients may prefer the safety and protection of being around only their immediate family or even being entirely alone over activities that involve a larger social circle, such as a book club or a bowling league. A study by Bergmark and colleagues (1999), for example, found that women who had cervical cancer were more likely than controls to be single. And in Navon and Morag's study of men receiving hormone therapy for prostate cancer (2003), they found that men avoided places where they would be expected to wear fewer clothes, like beaches and locker rooms. They deliberately demonstrated "masculine" tendencies, to distract others from their newly feminine physiques; declined social invitations so that they could avoid conversations about sex; and avoided any courtship of women that might be interpreted as having "serious intentions."

According to Judith Butler, many people think of coitus as the only "real sex" (Hawkins et al. 2009). Hawkins and colleagues conclude that when sexual intercourse ceases due to illness, patients and their partners also stop having other forms of physical contact because they can no longer experience the intercourse that used to be the pleasurable outcome of that foreplay. Patients therefore experience the loss of not only the pleasures of intercourse, but also those of mutual masturbation and other kinds of physical affection and support, losses that can impair their recovery.

Tanya was a 30-year-old woman with breast cancer who was stunning in her floral head scarf, but she came to the appointment without her boyfriend. She said that during her treatment, they had not been able to have sex, and the most devastating part was that it had been their only form of intimacy. With that gone, she felt removed from him and hurt that he was unable to express love for her in any other physical form. His association between sex and intimacy was limiting their relationship, and she wondered whether the relationship could survive her illness.

These changes in sexuality and intimacy are shared by the caregivers and partners of cancer patients. In a survey of 122 caregiver-partners of people with a wide variety of cancer diagnoses, Hawkins and colleagues (2009) found that 28 percent of men and 47 percent of women caregivers reported that their role led to a "repositioning of the person with cancer as a patient, non sexual, or a child" (p. 275). Several male caregivers reported that they felt sex was inappro-

priate with their ill partners because they had become accustomed to seeing their partners as children in need of care.

Fertility and Reproduction

Women and men undergoing treatment for particular types of cancer (for example, testicular, ovarian, or uterine cancer) may have serious concerns about the effect of the treatment on their fertility and reproductive abilities. It is therefore helpful to give them and their partners very specific information about the possible damage to their reproductive systems, along with any preventive steps they can take (such as banking sperm and eggs). You can offer this information regardless of the patient's age, sexual preference, relationship status, or the status of the disease.

Positive Changes

Some research shows that people's sexuality and intimacy changes for the better during or after they discover they have cancer. Some women with gynecological cancer reported less painful intercourse after surgery and, choosing to look on the bright side, were relieved that they no longer had to worry about birth control (Bourgeois-Law and Lotocki 1999). Hawkins and co-authors (2009) note that some partners felt increased understanding, acceptance, affection, devotion, and closeness. Some patients in Navon and Morag's study (2003) found that they became more considerate and better companions.

Mary, a 67-year-old woman with gastric cancer, always welcomed the team with a warm smile and quick wit in the mornings. When speaking with me alone about her thirty-five-year marriage she reported, *"Who knew that getting cancer would be one of the best things to happen to my marriage?! We had been living side by side for years and had really come to take one another for granted. Now, every day we make sure to say 'I love you' and cuddle together whenever we can."*

Clinician Barriers

Given the significance of sexuality in patients' lives, why is it that we as clinicians rarely include sexual issues in our assessments? We may believe that, since they have a life-threatening disease, these patients find sexuality of less importance, or that they are simply too sick to be interested in sexual activities (Saunamaki et al. 2010). As mentioned earlier, many of us believe that patients would

raise the subject themselves if it mattered to them, and we assume that silence indicates that it doesn't.

Some of us may want to discuss these issues with our patients but are not able to because of time constraints. Leslie Schover (1999) found that in managed care, more cancer survivors are followed by family physicians who may not have a full understanding of "long-term side effects," or who are not allowed to see patients only for "mental health treatment of sexual dysfunction." In inpatient settings, patients rarely see the same physician over time, and concerns and interventions may not be passed on from one to the next (MacElveen and McCorkle 1985).

Another problem is that current educational curricula often don't adequately prepare us for discussing sexuality and intimacy with our patients. In one study, nurses expected training on sexuality and did not feel responsible for pursuing the knowledge or educational programming on their own (Price 2010). A survey (by Mosher in 2005) of U.S. and Canadian medical schools revealed that more than half of the 101 responding schools provided only between three and ten hours of sexual medicine training, and just a third provided more than eleven hours (Shindel et al. 2010). Of the time that has been devoted to sexuality in medical schools, much of the focus has been on sexually transmitted infections, prostitution, unwanted pregnancies, infertility, menopause, and erectile dysfunction rather than on issues such as sex throughout the life cycle, effects of illness or medication on sexuality, and sexuality and aging (Karlen and Moglia 1995). In fact, the most powerful reason for physicians' lack of comfort in assessing their patients' sexuality is their perception of inadequate human sexuality training in medical school.

Another barrier is concern about how our patients will perceive us if we attempt to bring up this subject; will we be seen as disrespectful, insensitive, intrusive, or flirtatious (Schover 1999)? These concerns are particularly strong when we take care of patients of the opposite sex, in an age group different from our own, or from a different cultural background (Price 2010). Some of us may worry about where the conversation might go once it has begun or how we might end the conversation (Price 2010). Some simply may not feel equipped with answers or the right language.

Finally, we may be personally uncomfortable with discussing sexuality, and our own experience may become a barrier in our professional work. Unlike typical medical training, in my field of social work, we are asked to spend a great deal of time reflecting on our own beliefs, prejudices, upbringing, and biopsychosocial makeup. This encourages us to be aware of the assumptions we

bring into the room with our patients and to work on balancing those beliefs with the needs before us. It helps us to open our minds and provide more comprehensive care.

If you haven't had a chance to reflect on these subjects, you can use the list below (adapted from Price 2010) to test some of your own assumptions and hesitations around the subject of sexuality and its effects on your work. I've left some blanks at the end so that you can add any others that apply to you.

ASSUMPTIONS AND HESITATIONS ABOUT CANCER AND SEXUALITY: SELF-ASSESSMENT

- I do not feel adequately educated in this area.
- The concept is complex, and I wonder how far discussions could or should extend.
- My upbringing has taught me that it is impolite to inquire about sexuality.
- Sexuality is not routinely discussed in relation to health so I feel as though I am prying.
- I am not sure what cues the patient might use to signal a readiness to discuss sexuality.
- I am worried about what the patient might ask. What if they confide things that seem abhorrent or even illegal?
- It's difficult to find a private place for discussion, and I fear embarrassment.
- If I draw on my life beliefs, this might upset the patient.
- I don't believe it is as important to discuss sexuality if the patient is not in a relationship.
- I think that discussion of sexuality is dependent on the age or illness stage of patients.
- I am not at all sure how to have a discussion with a patient whose sexuality, lifestyle preferences, and assumptions seem ambiguous.

Other:
Other:
Other:
Other:

If you want to try a more open-ended exploration of your comfort level and attitude about sexuality, consider discussing these questions with a colleague or friend (Shell 2007).

DEEPER EXPLORATION OF ATTITUDES TOWARD SEXUALITY IN CANCER PATIENTS

Level of Comfort

1. How comfortable do you feel discussing sexual matters?
2. Notice physical tension, body position, eye contact, and facial expression when listening to specific sexual content. What makes you feel uneasy?
3. What sexual terms can you comfortably use to describe sexual fantasies, interest, arousal, orgasm, and behaviors? Try describing these experiences to a colleague.

Attitudes

1. List three values you have about sexual behaviors.
2. How would these values affect the way you would work with clients/patients whose problems reflect a conflict with your values?
3. List any areas regarding sexuality that are unacceptable to you.
4. What could you do to compensate for your attitudes if a patient presented something in one of these areas?

How to Approach the Subject

Mutual Explorer

This is not as scary as it sounds. There are many frameworks through which we can learn more about our role in discussing sexuality and intimacy issues, but one of my favorites is offered by Bob Price in his 2010 article "Sexuality: Raising the Issue with Patients." He invites us to accept the role of "mutual explorer" and states that "expertise develops . . . with facilitation of discussion rather than the sharing of knowledge" (p. 35). This approach allows us to learn as we go, admit when we don't know something, and keep our patients' needs at the forefront of the conversation. We don't need to expect to "fix" anything, especially if we don't have ready answers. Instead, we can help our patients explore or express their own needs. If you wait until you feel expert enough to answer every question, you're likely to find yourself continuing to avoid the subject altogether (Clifford 1998).

Here's an example of what a typical conversation might sound like, if you raised the subject early in your relationship with the patient:

You: *Many people who are dealing with cancer or going through treatment notice some changes to their sexuality or their ability to be intimate. Is this something you have noticed or are worried about?*

Patient: *Well, I'm not sure. But I know my wife and I haven't really been able to be intimate since this back pain started about three months ago.*

You: *Is that different from before the pain started?*

Patient: *Before my back, we would be intimate at least once a week.*

You: *Is this change something you have been able to talk about together?*

Patient: *Um, not really. We've been focused on other things and haven't stopped to discuss this. Will we be able to resume our previous level of activity together?*

You: *As your pain gets better, it is very likely that you will be able to. Most people are able to resume sexual activity given time, though sometimes they need to learn how to adapt to the changes brought about by the cancer or its treatment. As you know, we plan to start chemotherapy after your radiation therapy is done, and that could affect your sexual relationship. I will let you know about the aspects I am familiar with (particularly before beginning any treatment), but I need to know from you what changes you notice as the treatment proceeds. If there are answers I don't have, I will try to find them or connect you to colleagues and resources that can provide you with the information and support you need.*

Notice that you don't need to promise that you know all the answers, just that you are committed to discuss any changes and concerns with the patient and to provide access to other sources of information.

Competencies

Ideally, one of the members of your office staff or the practice you work in will be a reliable source of information in issues of sexuality (Schover 1999). For those interested in more training, important skills to learn would be providing education about the effects of illness on sexual functioning; suggestions on resuming sex comfortably and improving sexual communication; advice on how to mitigate the effects of physical changes—such as having an ostomy—on sexuality; and self-help strategies to overcome specific sexual problems, such as pain with intercourse or loss of sexual desire. As part of the information sheets you provide to patients and their families before they start treatment, include the side effects that could affect their sexuality so that they are informed well before they have to make a treatment decision (MacElveen and McCorkle 1985). Giving information in this way improves sexual outcomes (Carr 2007). Later in this chapter, I explore the ways in which an interdisciplinary team or a good referral list can provide the important information patients and their partners need.

Timing

Ideally, as you become more comfortable discussing sexuality and intimacy, you'll take a short baseline sexual history for every cancer patient prior to treatment (Bourgeois-Law and Lotocki 1999) and build on that at later visits. Questions may not come up the first time you approach this subject with patients. Early on in your relationship with them, patients may be so afraid of dying, or may have such high anxiety, that the subject of sexuality fades into the background. Often it is merely enough to let patients know that we are open to discussing issues of sexuality at any time.

A brief discussion over one or two visits is all most patients and partners with concerns about sexuality need. Because sexual problems often become more apparent or distressing during the first months after finishing active treatment, incorporate these questions into your routine follow-up appointments (Schover 1999).

Humor

How about using humor? Several books for patients address the crazy aspects of cancer and the benefits of laughing about them regularly. Any local or online bookstore can provide a wealth of resources on this topic. Sexuality can be one of the most inherently awkward and therefore most amusing subjects within the cancer experience. But we need to walk a delicate line if we use humor, being careful not to minimize a patient's experience inadvertently or introduce any lewd or inappropriate suggestions while still remaining open to the humor of the situation. Using our "mutual explorer" model, we can inquire about whether our patients or their partners have been able to use humor to cope. Some use humor to show their resilience and willingness to laugh at parts of their experience.

One young patient opened his wallet and revealed that he carried around a playing card with a big C on it, reporting that he "played the cancer card" often. *"You need help moving? Nope sorry, I got this here cancer." "Your unattractive cousin needs a blind date? Wish I could, but I've got cancer, see my card?"*

Models and Tools

If you're the kind of person who likes a framework as a mnemonic, here are two of the most popular models on how to address sexuality and intimacy. In the next section, I'll give you practice language. The articles in the bibliography by

Shell (2007), Katz (2005), and Cagle and Bolte (2009) will be of great help to those who want to learn more about these models.

PLISSIT

PLISSIT (Permission, Limited Information, Specific Suggestions, Intensive Therapy), created by J. S. Annon in 1976, is one of the most famous and widely used tools for addressing sexuality with patients (Table 8.2). It has been criticized for suggesting referrals for counseling or a sexual counselor (Hughes 2000), but only a small percentage of patients are likely to require outside referral.

BETTER

BETTER (Bring up the topic, Explain, Tell, Time, Educate, Record) was developed by Mick and Cohen in 2003 (Table 8.3). Cagle and Bolte (2009) suggest that although this model may be a useful tool to guide documentation, it might not place enough emphasis on more extensive counseling or referrals to other clinicians when needed.

Written Surveys

You can easily get literature on sexuality and cancer for your waiting rooms, including the American Cancer Society booklets for men and women on sexuality (see Schover 2006, 2009). If you want something more comprehensive, Table 8.4 lists a few selected valid and comprehensive assessment tools and surveys related to sexuality that are easy to interpret and that your patients can complete while they are waiting to see you.

Practice Suggestions

Language, Practice, and Setting

"But," you are likely asking, "how do I actually do this? When I am sitting across from my patient, what do I say that won't make us both feel awkward?" In the sections below, using the guidelines in the Practice Points box, I offer specific language (*in italics*) and suggestions for how to conduct the interview. I have drawn from several sources (Hordern and Currow 2003; Katz 2005; Spaulding 2006; Shell and Smith 1994; Shell 2007; Davis 2009; Cort et al. 2004; ARHP 2008) including my own practice experience.

PRACTICE POINTS: HOW TO APPROACH THE CONVERSATION

- Ensure privacy and confidentiality during the conversation.
- Introduce and normalize this topic as a routine part of cancer care.
- Address sexual concerns early and throughout treatment.
- Use open-ended questions and determine patient concerns and goals.
- Avoid overreaction and use a nonjudgmental approach.
- Do not make assumptions; stay open and curious.
- Do not use medical jargon.
- Refer patients with complex problems.

(Adapted from Shell 2007 and Hordern and Currow 2003)

Privacy and confidentiality. Make sure to close doors or pull curtains and minimize interruptions. A private room is ideal. Try to find time to talk with the patient alone (sometimes this is most easily done before or after a physical exam). If the patient has brought a partner to the visit, this time alone will allow you to assess the patient's perceptions of safety in the relationship. After you've introduced the subject, ask permission to include the partner in the conversation.

Along with everything else I will be discussing with you, I would like to answer any questions about how your cancer treatment may affect your feelings of intimacy and your sex life. Would you like us to include your partner in these conversations? Would you feel comfortable if [X] *joined us?*

If the patient declines, continue the conversation in private, asking, for example:

Do you feel safe in your relationship?

Do you have particular concerns about discussing issues of sexuality in front of your partner?

If any patients raise concerns of violence or coercion, refer them to a mental health professional with experience in intimate partner violence. Do not try to handle it on your own.

There are many potential benefits to including the partner if the patient feels safe doing so. First, in the role as caregiver, the partner may be experiencing changes in their sexual relationship and have no other outlet for exploring these issues or other opportunities to be educated. Second, having both partners in the discussion with you encourages and models more open communica-

tion between them. Finally, two sets of ears are better than one for remembering what you've told them.

Introduce and normalize sexuality, early and throughout. To set patients at ease while you're asking about sexual health concerns, try a nonverbal technique such as making direct eye contact and presenting an open and relaxed body posture (Cagle and Bolte 2009). Use what Gochros (1986, p. 14) calls "attending behavior," which includes "leaning slightly forward towards the client, listening to and remembering what the client says, giving verbal and facial indications that you are hearing and responding to the client's comments, and using a voice which conveys warmth and understanding."

Here are examples of language you can use to introduce or address the topic of sexuality:

- *Many people find that aspects of their sexuality and intimacy change as a result of cancer or related treatments. Some of these changes can affect relationships with others and some affect how we view ourselves. These changes can be just as distressing as pain or nausea, and I want to know whether you're experiencing any problems in this area that you want to discuss with me.*
- *Some people who are going through an illness like yours have been concerned about their sexuality.*
- *Women undergoing this procedure often have questions or concerns about intimacy or sexuality. Are there any concerns you would like to talk about?*
- *I ask these questions of everyone. I want you to feel comfortable discussing these matters with me at any point, even if you do not want to discuss them now.*
- *Do you feel that your sexuality has changed since your diagnosis?*
- *Other women who have been given this treatment have experienced some pain during intercourse.*
- *Some men taking this medication have problems getting or maintaining an erection.*
  What questions can I answer about how your medication will affect your sexuality?
- *Since your* [surgery / diagnosis / chemotherapy / radiation therapy], *do you feel any different as a* [man/woman]*?*
- *Some people find that their sexual feelings change when they go through this treatment. What about you?*
- *Is there anything you need to discuss regarding your sexual function?*
- *Tell me about any sexual changes you have experienced since the* [procedure/intervention].

Stay open and curious. Of course, it is critical that we avoid making assumptions about partner status or gender preference (Cort et al. 2004). In many states, same-sex couples cannot marry, so using "partner" instead of "husband" or "wife" will allow your patients to feel safe as they describe to you the unique circumstance of their intimate or sexual relationships (Cagle and Bolte 2009). Also, do not assume that your patient is exclusively with one partner, even if married. Even when patients do not have partners, that does not mean that they are not interested in discussing their concerns about sexuality.

Are you currently involved in a sexual relationship?
Do you have sex with men, women, or both?
How has your illness affected your close relationships?

Avoid medical jargon. Be direct when educating or giving suggestions:

- *While you should not have* vaginal *sex until you have had your 6-week postsurgical check-up, it is fine to kiss and cuddle with your partner. Don't worry if you find yourself becoming aroused. This is not harmful and will actually speed healing.*
- *If you find penetrative intercourse painful, you may want to suggest to your partner that you use a side-by-side position, or that you be on top. This will lessen the chance that you'll experience pain. There are also such alternatives as mutual masturbation and touching.*

Refer for complex problems. When patients present complex problems, I have no hesitation about referring them for expert help. Any mention of sexual abuse, violence, control, fear, or harmful practices, for example, are red flags for referrals. A sexual therapist is also the right person to handle any issues that connect to long-standing sexual problems.

- *It sounds to me like the sexual abuse you describe has had long-lasting effects on you. I'm glad that you were able to share this with me. I would like to refer you to Dr.* [X]*, who is an expert in this area and who would take on your care along with me so that you get the help you need to deal with these issues.*
- *I can hear that the sexual concerns you had with your wife prior to your cancer diagnosis have only magnified since then. Would it be okay with you if I identified for you the names of some counselors who specialize in helping couples with these issues?*

Listen for entry points. Even if patients say no to initial questions about sexual concerns, they may provide cues to the contrary during their visits with you. Often, there are "entry points that provide openings to conversation and give

clues to areas of concern such as 'He just doesn't seem to love me anymore' or 'I just look so ugly' " (Cort et al. 2004, p. 351). We may feel tempted to retreat and reassure them or to change the subject to avoid our own discomfort ("*I'm sure he still loves you*"; "*Oh no, you're not ugly*"). Resist that temptation, and explore further:

What makes you feel like he doesn't love you anymore?
Are there ways in which your relationship has changed since the cancer?
Tell me what makes you feel ugly.

Suggestions to Address Sexual Concerns

Whether still in the midst of treatment or beyond it, patients are often anxious about engaging in or resuming sexual activities (Schover 1999). You may wonder what kinds of suggestions you should offer to your patients once you have identified and explored their sexual concerns. Many researchers (Cagle and Bolte 2009; Schover 1999; Cort et al. 2004; Hordern 2000; Gianotten 2007; MacElveen and McCorkle 1985; Hughes 2000) offer helpful suggestions that I have grouped into what I hope are useful categories in Table 8.5.

Although patients often want information, sometimes they simply want to be heard. If you "reflect back" what they just said, they're more likely to feel understood; then ask follow-up questions to help you assess how problematic these issues are for them.

- *It sounds like your level of fatigue has really caused some challenges for you and your girlfriend's sex life.* [Pause.] *Is this something that it would be helpful for us to brainstorm about?*
- *I can hear how strange it is for you to look down and see that scar. Is this something that might affect your thoughts about dating?* [If yes]: *Do you think you would like to talk further with someone about this issue?*

Wrapping Up

Wrapping up this discussion of sexuality and intimacy can be as simple as saying thank you, summarizing, emphasizing your presence, being candid about time limitations during this visit, offering the support of other team members, or setting expectations for duration of symptoms.

- *Thank you very much for sharing these things with me. It is important that I understand all the ways in which this treatment is affecting you so that we can work on them together.*

- *So it sounds like the nausea has made it difficult to be as intimate with your wife as you would like. Let's try the antiemetic medication that I suggested and follow up during our next visit to see whether it has made a difference.*
- *I can hear how isolating it has felt for you to be going through this experience. I want you to know that* [I / our team] *will continue to be available to support you through this illness.*
- *I am aware of the time and want to make sure that we have a chance to talk about your next chemo treatment too. Perhaps we can continue this discussion at our next visit?*
- *I wish we had more time to discuss this right now, but your infusion is in ten minutes, and we still need to review this paperwork. Would it be OK if we asked your nurse* [X] *or your social worker* [Y] *to continue this conversation with you once you get set up with the IV?*
- *It seems like the pain from the surgery has continued to make intimacy difficult for you and your partner. I know this time can be so hard, but I also want you to know that it won't always feel this way. The pain should subside within* [X time], *and you will begin to feel better. Most patients report being able to return to their daily activities within a few weeks, and that includes sexual activities.*

Special Considerations

Although stereotyping a patient's sexual experiences by culture, race, age, or severity of disease is never helpful, being informed in general about the influences of culture race, age, or severity of disease on attitudes toward intimacy and sexuality can be. Below, I offer some thoughts about the effects of these factors. Readers interested in learning more about any of these topics can use the resources listed in the bibliography.

Culture

The literature on culture and sexuality in oncology is relatively thin. Shell (2007) offers us a brief summary of cultural considerations in African American, Asian American, and Hispanic cultures that may influence the lives of our patients and help guide our questions. But someone's "culture" is much more than their ethnicity or race; it also includes socioeconomic status, education level, community norms, geographic identities, and family patterns. Awareness of culture

may make us more wary of addressing issues of sexuality, but with a respectful curiosity and open-ended questions, we can cautiously assess the effects of a person's culture on their sexuality.

Similarly, the "culture" of medicine may differ across practice setting, discipline training, and geography. This chapter is written by a female American social worker and edited by a female American physician. We practice with our colleagues in a large academic hospital in Boston, and our suggestions are likely not to be universally applicable to every medical environment or context. We count on you to adapt our suggestions to serve the patients and their partners and families whom you care for.

Same-Sex Partners and Sexual Orientation

As Judith Butler asserts, our culture typically places all sexual discourse in the "heterosexual matrix" (Hawkins et al. 2009). This essentially equates penetrative sex between a man and a woman with "normal" healthy functioning sex. If we also adopt this stance, or worse, are unaware that we hold this bias, we are likely to alienate any patients who do not live this way, or who are forced away from coitus because of their disease (Hawkins et al. 2009). Studies show that gay and lesbian cancer patients, not surprisingly, also experience changes to their sexuality. Indeed, one study found that four of six lesbian partners reported complete cessation of sex after cancer (Hawkins et al. 2009).

Gay, lesbian, and transgendered people face numerous concerns about stigma even before they get cancer, and they may not feel comfortable disclosing their sexuality or sexual practices with us for fear of judgment. When we use non-neutral language or make assumptions about sexual preference or marital status, we may be amplifying these fears and making it impossible for our patients to share their concerns about sexuality with us. The standard choices in hospital registration forms, for example—single, married, separated, divorced, or widowed—do not reflect the lifestyles of most partnered gay men and lesbian women or those of unmarried heterosexual couples (Katz 2009). Similarly, "most educational material" given to patients and most posters displayed in hospitals and clinics contain few, if any, images of same-sex couples; "even these minor details may influence their comfort in disclosing sexual orientation" (Katz 2009, p. 207).

Women and men in same-sex relationships often feel compelled to love in secret and thus may not receive the same degree of support that their heterosexual counterparts do. They frequently feel obliged to step aside publicly when

health professionals address traditional family members as primary caregivers (Hordern 2000), and in most states, they are not protected by law as "legitimate" partners. Imagine the impact of not having your primary loved one present at your most vulnerable times.

Some strides have been made for partners of gay and lesbian federal employees who can now have access to family and medical leave, counseling services, and visitation with their loved ones when hospitalized. Similarly, some states have made advances in this area. If we can recognize the limitations that many of our patients face, we will be open to learning who is important in their lives and can advocate for them if we need to.

Gay and lesbian patients have also reported experiencing higher stress associated with diagnosis and treatment of illness, lower satisfaction with care provided by physicians, and lower satisfaction with emotional support from health care providers (Katz 2009). The gay male community may be concerned that society will misinterpret the manifestations of their cancer as arising instead from HIV/AIDS (Katz 2009) and "judge" them accordingly. Older gays and lesbians who continue to live in communities that do not support gay rights can often remain hidden from one another and feel isolated (Horsley and Anike via Hordern 2000). We can help by making available to them the names and contact information of gay-friendly or gay-identified counselors, support groups, and online supports (Katz 2009).

Aging

If cancer and sexuality are awkward for practitioners to discuss, having those discussions with older patients who could be our parents can create a perfect trifecta of discomfort. Since more than half of all cancer diagnoses occur in people over 65 years of age (Shell and Smith 1994), and some estimates state that by 2030, as many as one-fifth of people living in the United States will be over 65 (Karlen and Moglia 1995), we'd better get busy working through our discomfort.

Mr. R was a 73-year-old man who was hospitalized with complications of prostate cancer and whose wife was consistently at his bedside. One day after a long conversation, I told them that I would leave and give them some alone time. He smirked and said that I *"had better do that since he and his wife hadn't had the chance to have their daily conjugal yet."* He quickly followed by saying he was joking, but that *"people assume that just because we have wrinkles, we don't still take pleasure in one another . . . but we do."*

Shell and Smith (1994) believe that "recognizing the need for and encouraging an open exchange about sexual issues is paramount with elderly people, who experience not only the natural progression of aging but also the difficulty of dealing with cancer" (p. 553). Elderly patients battle external and internalized myths about their own sexual interest and face the loss of partners, decreasing privacy, and often loss of dignity as they increasingly rely on assistance from others. As the saying goes, "Aging isn't for sissies." Add to that a diminishing social network, mobility problems, other health challenges, and, often, partner illness or dependence.

Shell and Smith offer a detailed list of suggestions and interventions that we or our nurses, nurse practitioners, or social workers can incorporate into our practice with elderly patients (1994, p. 557). These include screening for depression and anxiety, which can decrease their ability to feel sexual; assessing their precancer sexual functioning; and reassuring them that we understand that sexuality can be an important component of their relationship. Changing positions and locations for sexual activity can be a way to cater to aging bodies and monotony. Shell and Smith agree that we should broaden the definition of sexuality to indicate sharing, intimacy, and communication, as well as endorsing good nutrition, sleep, exercise, and self-care. They also recommend the American Cancer Society's *Look Good, Feel Better* program and a book called *Beauty and Cancer,* by Noyes and Mellody (1992 edition).

We may need to start by educating ourselves. In a survey of sexual health educators, Karlen and Moglia (1995) reported that most respondents used negative terms such as "limited," "uninformed," and "terrible" to characterize medical students' knowledge of sexuality and aging, though one would hope this has improved in the past fifteen years. If you are an educator, you might use films such as *A Ripple in Time* (featuring interviews of older people and sexuality), small group discussions, practice with taking an older person's sexual history, and having elderly people speak with students, residents, or fellows about their sex lives.

Partners

There is often little formal acknowledgment of the sacrifices partners make or the ways in which their lives change to accommodate the needs of the patient; even less so of the ways in which their sexual needs are altered. Medical providers, literature such as brochures, hospital systems, and even patients themselves can ignore the experience of loved ones. Even if partners provide support lovingly and willingly, they may still struggle with what the illness takes away from them. In the same way patients can lose sight of the wholeness of their

identity while sitting in a hospital bed, a partner can feel distilled down to the role of caregiver. One man I worked with said, *"I love my wife, but I miss being her husband."*

One study by Kuyper and Wester (1998) looks at the ways in which companions experience an altered identity: they have become a partner with an ill person and can no longer structure their daily lives based on their previous interests or social activities as a couple, which include, of course, their sexuality and intimacy. Partners can report feeling trapped or worried that they are being selfish if they tend to their own issues or desires.

Couples can begin to struggle if both the patient and partner pay attention only to the patient's needs and concerns, and neither gives energy or attention to the partner's needs, including sexual desires. In the Kuyper and Wester study, some partners "said they did not want to discuss [sexual matters with the patient] as they did not want to create feelings of guilt in the patient" (p. 245). Moreover, partners often "had no contact at all with the treating doctor," were "insufficiently informed about the possibilities they have of supporting the patient during examination and admission in the hospital" and subsequently experienced feelings of "fear and of powerlessness" (p. 246). We've already explored the ways in which direct communication between patients and clinicians helps address and allay concerns around sexuality; the same applies to their loved ones.

Partners of cancer patients also face new and unaccustomed tasks, such as being the sole wage earner or insurance carrier, which can lead to significant financial losses; what time remains in the day may now be filled with parental duties and caregiving. Partners can easily find themselves developing stress, burnout, and fatigue as well as feelings such as loss, frustration, isolation, and resentment; communication between couples can become strained. It is not hard to imagine the effect this could have on a person's feelings of warmth, intimacy, and sexual desire.

One middle-aged caregiver I worked with said, *"I try to prioritize all the needs of our household and spend my day raising our children, going to work, doing the bills, picking up prescriptions, and the minute I walk in the door, she jumps on the things I haven't done yet. It is driving a wedge between us."*

As partners watch a loved one face the threat of death, they may also find themselves contemplating their own mortality and confronting the meaning of their lives (MacElveen and McCorkle 1985). And when they most need support, the bulk of attention is usually focused on their sick mate. Even their own friends and family may fail to recognize that they have their own needs outside a partner's illness and may unreasonably expect that they constantly be at the patient's bedside and never take time for themselves. The distress, anger, and

sadness they may feel can all affect sexual functioning and their desire to be intimate with their partner.

One woman whose husband had colorectal cancer told me angrily, "*You really find out who your friends are when you go through something like this. Friendships I thought were solid have just disappeared. I no longer have people to talk to, and it makes me feel bitter and alone. Sometimes it makes me resent my husband because he is the focus of everything. Sometimes I just pull away from him because I don't know what to do with all of these feelings.*" Having the opportunity to explore these feelings with a social worker or other mental health or spiritual counselor is likely to benefit both the partner and the relationship as a whole.

After one session, a couple who had been experiencing frustration and difficulty communicating told me they felt relieved that they could finally voice their opinions. During our talk, the patient had become aware of how centered their lives had become around his illness and ways in which his partner would benefit from more balance. His partner acknowledged that he needed to communicate his frustrations more often rather than keeping them bottled inside or assuming that the patient should read his mind. The energy between them shifted from tense and distant to more open and compassionate. Where the session had started out with them on opposite ends of the couch, it ended with them clasping fingers and moving closer.

Single People

As difficult as a cancer diagnosis can be for a couple to navigate, single people with cancer also face significant challenges. Patients who do not have a partner with whom to share the illness experience may feel a lack of support and intimacy, doubts about the possibility of future love, and difficulties with the concrete tasks of making it to doctor's appointments and functioning while ill. There can also be "strong inhibitors to the establishment of intimate relationships with a partner" (MacElveen and McCorkle 1985, p. 59).

Sarah was a 26-year-old breast cancer survivor who said that, even though her cancer was many years in the past, she still could not imagine a partner being able to love her with all her physical and emotional scars. She reported feeling uncomfortable with how to approach the subject in dating situations, so she avoided these situations. Additionally, she felt that her cancer experience, while remote, remained intense and relevant in her current life, and she worried that new partners would minimize or fail to understand the power of this history.

Research supports Sarah's experience and has found that seeking new relationships can cause stress for cancer patients, particularly around the idea of when to disclose their history of cancer to new potential partners (Hordern 2000). When entering a new relationship, researchers say "the potential partner needs time to absorb information about cancer and its consequences," and "the woman herself needs reassurance" that "a strong, mature relationship can be expected to handle this kind of issue" (MacElveen and McCorkle 1985, p. 59).

For single young adults with cancer, illness often pauses their lives at a time when their peer group is meeting new people, finding partners, and forming families. Ellen was a 30-year-old woman with sarcoma who said, *"I feel more lonely when I go out with my girlfriends now. They discuss who they are dating or engaged to and my only news is my next line of chemo. It is easier to just decline when they ask me to go out with them."*

You might encourage these patients to talk to some of their friends about their feelings and to find new friends, including other young adults with cancer. Some of the websites that offer online support for these patients are listed at the end of this chapter.

Palliative Care and Sexuality

Another myth is that patients who have advanced cancer or who are experiencing distressing symptoms are not interested in or capable of intimacy or sexual expression. Accordingly, "within palliative care settings, patients are rarely given an opportunity to share sexually-related issues with their health care providers" (Cagle and Bolte 2009, p. 224). This situation is only amplified by the misconception that we discussed earlier, that elderly adults, who make up 65 percent of those needing palliative care, are no longer sexually active and are not interested in intimacy issues (Hordern 2000).

Loving relationships, intimacy, and sexual contact are still very important to patients and their loved ones during terminal illness, and sexuality can be an important aspect even in the last weeks and days of life (Gianotten 2007; Hordern 2008). But as you might expect, the form that sexuality takes at that time shifts somewhat, often becoming centered on "emotional connectedness" and "intimacy through close body contact, hugging, touching, kissing, hand holding, and eye contact" (Lemieux et al. 2004, p. 634).

In comparison with other cancer patients, "palliative care patients reported the greatest difficulty with sexual function" (Ananth et al. 2003, p. 203—NB: Ananth uses "palliative care" in its older, very narrow meaning, to refer to patients

with refractory, advanced disease). The types of sexuality problems listed by these patients include poor or changed body image, altered sexual functioning as a result of anxiety and depression, fear of rejection, poor communication, loss and grief, bereaved partners coping with loss of interdependence, and changes in family roles (Cort et al. 2004). For some, "memories from the past can pop up," either "unfinished business like missed sexual opportunities, or jealousy regarding real or supposed extramarital relations," and "in some couples the sexual future of the surviving partner" becomes a focus (Gianotten 2007, p. 302).

For many patients with advanced cancer, however, continuing sexual connection can provide "energy, physical and emotional relaxation, pain-relief, better sleep, togetherness, consolation, comfort, self-esteem, or better coping with heavy emotions" (Gianotten 2007, p. 302).

Mr. B was a 55-year-old patient with gastric cancer. He and his wife had asked me to educate them about home hospice supports. They mentioned needing a hospital bed for the living room when his wife said tearfully, *"That's the worst part, not being able to sleep together at the time when we need each other most."* We brainstormed ways for them to still sleep near or with one another, and to prioritize hugging, kissing, and cuddling, which they both reported missing during the last months of his illness.

The Inpatient Setting

In my role as an inpatient palliative care social worker, I have found that for several reasons, the inpatient setting makes it difficult to bring up the topics of sexuality and intimacy with my patients. Often, the issues that bring cancer patients into the hospital are acute enough that the initial part of their visit is focused on treating their pain, nausea, dyspnea, and so forth. The idea of asking a patient in those circumstances to reflect on how her sexuality has changed as a result of her cancer can seem insensitive, ill-timed, and inappropriate. When, as sometimes happens, our patients have to share a room with another patient, privacy is limited, and doctors and nurses and nurses' aides are always walking in and out at random intervals. Also, the realities of today's medical care are such that as soon as patients begin to feel better, they are discharged. For all these reasons, the outpatient setting might appear to be better suited to conversations about sexuality and intimacy.

As with other sensitive topics, however, no matter the setting, I try to invite patients to let me know if these issues are important to them. They might arise

as patients try to decide whether or not to have an intervention (for example, a g-tube or an epidural catheter) that could affect their ability to be intimate or to experience pleasurable sensations. If a procedure such as a nerve block might cause numbness or decreased sensation in sexual organs, that important potential side effect can easily be included in the discussion of the risks, burdens, and benefits, beginning with a simple question such as *"Do you have any questions about how this procedure might affect your sexuality or ability to be intimate?"*

Physical touch and intimacy can be extremely therapeutic and can be encouraged even in the inpatient setting. Remarkably, even in the sterile, chaotic environment of the hospital, patients often still need intimacy or sexual fulfillment. We can at least give permission for partners to lie in bed with their loved ones or for patients and their partners to close their doors or be "undisturbed" for a period. We can be open to the possibility that a request to leave the hospital for a few hours to go home may be a request to have sex with their partner or to masturbate, a request patients may be too embarrassed to make directly. Other ways in which we can advocate for our hospitalized patients are listed in the paper by Cagle and Bolte (2009).

Interdisciplinary Practice and Referral List

If we had a wish list and donors willing to support the salaries of team members who were expert in the issues of intimacy and sexuality of concern for our patients and their partners, what should it include? Leslie Schover, who has written extensively about cancer and sexuality, provides suggestions for the resources and team members needed at comprehensive cancer centers (1999). She suggests that smaller cancer centers that do not have the funding to offer all the needed specialists on staff build a referral network that includes experts in the areas described below.

Comprehensive Cancer Centers

Every comprehensive cancer center would ideally offer specialized education and resources about cancer-related sexuality concerns, such as sperm banking, cryopreservation of ovarian tissue, contraception, hormone replacement therapy, infertility therapy and options, and high-risk obstetrics for pregnant cancer patients. Unfortunately, these services do not pay for themselves, but they can markedly improve patient care and satisfaction.

An interdisciplinary team focused on sexual issues typically includes the following clinicians:

- *Mental health professional* trained as sex therapist, familiar with cancer and treatment issues as well as being sensitive to GLBT, age, and cultural issues
- *Gynecologist* well versed in issues of female sexual dysfunction, pelvic pain after treatment, fertility, and hormone treatment
- *Urologist or internist* who specializes in male health and is familiar with medical and surgical options for male sexual dysfunction
- *Palliative care clinician* who specializes in pain and symptom management to optimize daily functioning and energy, and in communication and eliciting goals of care that can be shared with the oncology team
- *Rehabilitation specialist* to help patients resume physical activity despite handicaps
- *Enterostomal therapist* to assist with making ostomy appliances less intrusive or unattractive
- *Respiratory therapist* to suggest sexual positions for patients who are connected to respirators
- *Physical therapist* to advise on issues such as whether to wear a prosthetic limb during sex or best positions for sexual contact after a hemipelvectomy

If you are not certain what is available at your own facility, the clinical nurse educators, mental health professionals, patient navigators, social workers, or resource specialists are likely to know.

Summary

Sexuality and cancer is an area of medicine that, more than most areas, requires us to explore our own assumptions, biases, and areas of discomfort before we are likely to become comfortable or confident in having these discussions with our patients. We will be much better equipped to pick up subtle cues of concerns about intimacy and sexuality, and more helpful to our patients and their partners, once we have acquired this self-awareness. We can improve our practice if we increase our general knowledge about how cancer and its treatments can affect sexuality for patients and their loved ones and provide this information routinely as we do with the other risks and burdens of the therapies we offer. Providing a safe space for discussion, education, and access to resources, as well as being vulnerable and saying "I don't know" if something is outside our experience, go a long way. Let's work to feel more comfortable as we search for answers along with our patients and make a serious effort to help them improve this aspect of their quality of life.

Tables

Tables 8.1 to 8.5 follow on pages 418–422.

Table 8.1 Changes That Affect Sexuality and Intimacy

Causes	*Changes*
Cancer itself	Pain Fever Incontinence Nausea/vomiting Weakness
Surgical interventions	Anatomical changes or loss of genitalia and other body parts (mastectomy, testicles, ovaries) Pain Wounds/scars Ostomy or catheter placements Loss of sensitivity Penile and vaginal shortening CNS damage Incontinence
Chemotherapy and radiation therapy	Fatigue Nausea/vomiting Loss of sexual desire Decreased frequency of intercourse Pain Erectile dysfunction Changes to bowel motility Vaginal pain for patients or irritation for partners Hair loss (on head and body, sometimes causing feelings of being childlike) Premature menopause
Hormone therapy	Reduced androgens that promote sexual desire Hot flashes Night sweats Vaginal discharge Breast development and weight gain in men Loss of erotic dreams and fantasies Decreased libido
Medications used to treat pain, depression, and anxiety	Decreased libido Fatigue Suicidal ideation

Table 8.2 PLISSIT Model for Addressing Sexuality and Intimacy with Patients

P	Permission	Help patients and partners understand that you think their sexual health is important, that sexual concerns are legitimate, and that comprehensive cancer care includes addressing this issue. Let patients know that you will routinely screen for this issue and ask open-ended questions.
LI	Limited information	Educate patients about the ways in which their sexuality might be affected by the cancer or related treatments, how long these disturbances might last, and if there are red flags to watch for. Include written materials addressing these issues when they are available. Address any questions that patients broach.
SS	Specific suggestions	Depending on your proficiency in this area, you or a member of the interdisciplinary team might offer specific suggestions, including likely side effects of a patient's particular cancer course and practical suggestions for addressing them.
IT	Intensive therapy	If no one on your team is able to address a patient's questions adequately or the patient's experience appears to require more extensive conversation, this would be the time to make a referral. (Check the resource list for useful referrals.) One study by Derogatis and Kourlesis in 1981 estimated that only 30 percent of the cancer population will need this last level of intervention (Cagle and Bolte 2009).

Table 8.3 BETTER Model for Addressing Sexuality and Intimacy with Patients

B	Bring up the topic	Let patients and partners know that you want to talk with them about the ways in which their cancer might affect their sexuality and intimacy.
E	Explain	Help patients understand that sexuality is a part of living well and that sexual concerns are an important part of comprehensive cancer care.
T	Tell	Let patients know that you will help them find resources and clinicians who can address any concerns that may arise.
T	Time	Let them know that they may bring up issues of sexuality at any time.
E	Educate	Educate patients about the ways in which their sexuality will be affected by their cancer or related treatment.
R	Record	Include this discussion in the patient's record so that others will know it has happened.

Table 8.4 Sexuality Assessment Tools and Surveys

CARES	Cancer Rehabilitation and Evaluation System	P. A. Ganz, C.A.C. Schag, J. J. Lee, and M. S. Sim, The CARES: a generic measure of health-related quality of life for patients with cancer, *Quality of Life Research* 1:19–29, 1992.
FSFI	Female Sexual Function Index (19-item index)	R. Rosen, C. Brown, and J. Heiman, et al., The Female Sexual Function Index: a multidimensional self-report instrument for the assessment of female sexual function, *J Sex Marital Ther* 26:191–208, 2000.
FSFI a	Female Sexual Function Index validated for use in lesbian population	J. K. Tracy and J. Junginger, Correlates of lesbian sexual functioning, *J Womens Health (Larchmt)* 16:499–509, 2007.
IIEF	International Index of Erectile Function (15-item index)	R. C. Rosen, A. Riley, G. Wagner, et al., The International Index of Erectile Function: a multidimensional scale for assessment of erectile dysfunction, *Urology* 49:822–830, 1997.
IIEF a	International Index of Erectile Function validated for use in homosexual, HIV-positive men	K. Coyne, S. Mandalia, S. McCullough, et al., The International Index of Erectile Function: development of an adapted tool for use in HIV-positive men who have sex with men. *J Sex Med* 7:769–774, 2010.
PEDT	Premature Ejaculation Diagnostic Tool (5-item index)	T. Symonds, M. A. Perelman, S. Althof, et al., Development and validation of a premature ejaculation diagnostic tool, *Eur Urol* 52:565–573, 2007.
ISL	Index of Sexual Life (11-item instrument)	M. Chevret, E. Jaudinot, K. Sullivan, et al., Quality of sexual life and satisfaction in female partners of men with ED: Psychometric validation of the Index of Sexual Life (ISL) questionnaire, *J Sex Marital Ther* 30:141–155, 2004.

Table 8.5 Suggestions to Address Sexual Concerns

Safety concerns	• Reassure them that cancer cannot be spread through sex. • Let them know which sexual acts may come with risk for pain; e.g., during recovery from surgery, intercourse may irritate the surgical cut. • If they are immune deficient: —Avoid intercourse if the white blood counts are dangerously low. —Clear tracheotomies of mucus and cover them lightly during sexual activity. • The first 48 hours after chemo, couples should use condoms to protect against cytoxic waste that is present in blood and bodily fluids. • Reassure them that external beam radiation does not leave the body radioactive, nor do radiation implants once they are removed from the body.
Cosmetic interventions	• Aromatherapy minimizes odors (eucalyptus, peppermint, or coffee grounds). • Specialists in salon care, makeup, wigs, ostomy pouches or prosthetics, penile or breast implants may help improve patient appearance. • Wearing camisoles or scarves during sex can help cover stomas or scars.
Treatments / complementary therapies	• If sexual side effects are causing distress, review all medications and alter if possible. • Consider recommending Reiki, massage (except in patients with coagulopathies), exercise, aromatherapy, relaxation, meditation, yoga, and warm baths for comfort, mood enhancement, energy, or decompression. • Refer to mind-body work for connecting emotionally with changed physical landscape or self-concept. • For dryness, prescribe lubricants that are water based and estrogen- and perfume-free. • Kegel exercises may decrease incontinence in women. • Evaluate for need of antidepressants for mood or energy.
Sexual expression	• Encourage exploring alternative methods of sexual expression (such as masturbation, reading erotica) and reciprocation (such as fantasy, anal penetration, oral or manual stimulation). • Discuss different sexual positions or use of pillows to facilitate comfort. • Have partners show each other physically what they want. • Ask them to try removing penetrative intercourse from options initially and encourage couples to “do anything but.” • Discuss acts of intimacy and sensuality, such as washing, hair brushing, touch or massage with oils.

(continued)

Table 8.5 Suggestions to Address Sexual Concerns *(continued)*

	• Encourage them to strengthen the often blurry divide between dual roles of caregiver / lover and patient / lover by establishing a romantic environment: candlelight, music, wine, and dressing for the occasion.
Recalibrating expectations	• Help to align their expectations within the reality of the disease. • Let them know they made need to plan sexual activities like any other exertion, for example, if they need to take pain meds 30 minutes prior. • Help patients find a time of day when they have good energy. • Ask them to regard sex as time to share pleasure not to perform. • Urge partners and patients to discuss whether one may need to withdraw from the physical part of the relationship and give them "permission" to do that. • Ask them to resume sex gradually by looking at / touching changed parts of the body; nonsexual touching, massage, cuddling; then starting with manual or oral contact. • Acknowledge that it may take time to learn to love one's new body and to change past foreplay patterns or sexual positions, and that first attempts may be disappointing. • Encourage intimacy regardless of ability or desire to engage in sex. • Help people weigh the potential side effects of medications or interventions for sexual issues (getting implants may come with its own risks).
Communication	• Encourage more open communication between partners about sexual needs, either with a counselor or alone. • Have the couple establish ground rules and private time to talk. • Suggest that they review what has changed, what hurts, what excites. • Advise that they make specific, positive requests for change rather than criticizing current practices. • Encourage single people to rehearse a comfortable approach or explanation for any sexual issues that arise when dating and beginning sexual activity with new partners.
Referral	• When necessary, refer for the following: pharmaceutical interventions (vaginal lubricants, oral medications, contraceptive options); surgical interventions (penile or breast implants, injections, reconstructive surgery); hormone therapy; physical rehabilitation for major physical handicaps; therapy (psychosexual, intimate partner violence).

RESOURCES

If you want to educate yourself further, consult colleagues who incorporate sexual assessment into their practices, such as mental health counselors or sex therapists, and attend seminars or workshops designed to assist you in examining your attitudes, values, and beliefs about sex. Go online or contact your profession's national organizations for any current continuing education offerings on sexual health training.

The American Cancer Society (ACS) has several resources on sexuality and intimacy. ACS's comprehensive list of resources for patients and clinicians includes national websites, books (e.g., *Beauty and Cancer,* by Noyes and Mellody, 1992 edition), pamphlets, GLBT information, fertility resources, cancer- and treatment-specific guides, personal stories, and resources for sexual health professionals. To access these resources go to www.cancer.org and search "sexuality."

Sexuality: www.cancer.org/Treatment/TreatmentsandSideEffects/PhysicalSideEffects/DealingwithSymptomsatHome/caring-for-the-patient-with-cancer-at-home-sexuality

Sexuality for the Woman with Cancer (also available in Spanish and in pamphlet form): www.cancer.org/Treatment/TreatmentsandSideEffects/PhysicalSideEffects/SexualSideEffectsinWomen/SexualityfortheWoman/index

Sexuality for the Man with Cancer (also available in Spanish and in pamphlet form): www.cancer.org/Treatment/TreatmentsandSideEffects/PhysicalSideEffects/SexualSideEffectsinMen/SexualityfortheMan/index

The National Cancer Institute also has a vast array of information for health professionals and patients about cancer and sexuality in their Sexual and Reproductive Issues (PDQ) section.

For health professionals: www.cancer.gov/cancertopics/pdq/supportivecare/sexuality/HealthProfessional

For patients: www.cancer.gov/cancertopics/pdq/supportivecare/sexuality/Patient

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CHAPTER 9

Managing Other Distressing Problems

Psychological Problems
- Anxiety
- Depression
- Personality Disorders
- Counseling

Oral Problems
- Candida
- Herpes Simplex Virus
- Treatment-Induced Mucositis
- Xerostomia

Gastrointestinal Problems
- Ascites
- Diarrhea
- Dysphagia, Nausea, and Vomiting
- Treatment-Induced Nausea and Vomiting
- Malignant Bowel Obstruction–Induced Nausea and Vomiting
- Nausea and Vomiting of Unclear Etiology

Respiratory Problems
- Dyspnea
- Cough
- Hemoptysis
- Hiccups

Skin Problems
- Hand-Foot Syndrome
- EGFR-Inhibitor–Associated Toxicities
- Fungating Skin Lesions
- Pressure Ulcers
- Pruritus

Insomnia

Hot Flashes

Weakness and Fatigue

Eaton-Lambert Syndrome
Anemia
Metabolic Abnormalities
Anorexia and Malnutrition
Coping Strategies
Role of Hospice Programs
Role of the Palliative Care Team
Integration of Oncology and Palliative Care
Summary
Tables
Bibliography

Patients with cancer suffer from any number of disorders that cause distress without causing pain. This chapter focuses on the most common and most distressing of non-pain problems and their treatment. Palliative care and hospice teams (introduced in Chapter 4) are often involved in implementing these treatment plans. Their role is described at the end of this chapter, where tables also appear.

Psychological Problems

In 2003, the National Comprehensive Cancer Network (NCCN) first recognized the magnitude of the problem of psychological distress by issuing guidelines for the evaluation and treatment of cancer-related distress. The panel who prepared the most recent version of the NCCN *Distress Management Guideline* (version 1.2013) documented a cancer-related distress prevalence of 20 to 47 percent, and noted that fewer than half of these patients were referred for help. Panel members included representatives from all the disciplines involved in the delivery of supportive psychosocial services and counseling in NCCN institutions, including "oncology, nursing, social work, psychiatry, psychology, and clergy" (NCCN 2013, p. MS-3), along with a patient advocate. The guidelines offer proposed standards of care, screening tools (including a distress "thermometer" and checklist of practical, family, emotional, spiritual/religious, and physical problems), assessment and treatment algorithms for patients suffering from psychological distress (dementia, delirium, mood disorder, adjustment disorder, anxiety disorder, substance abuse, personality disorder), and indications for referral to psychiatric, social work, and pastoral services. In this section I review anxiety, adjustment disorders, major depression, personality disorders, and counseling.

Anxiety

Cancer patients often experience anxiety or depression or both together. All patients need time to recover from the initial shock of a cancer diagnosis, but by six weeks, 20 to 35 percent will have recovered their psychological equilibrium. Almost 50 percent of patients will continue to have an adjustment disorder, 10 to 20 percent an anxiety disorder, and 5 to 10 percent a major depression. Patients at high risk for anxiety include younger patients, women, patients with a history of substance abuse, and patients from lower socioeconomic strata (Stark et al. 2002). Anxiety often peaks during the initial cancer therapy, but it can persist for as much as a year, even when the patient has had a curative procedure. Anxiety lessens during adjuvant chemotherapy but peaks again at the cessation of the therapy, falling gradually as the remission lengthens. If the cancer recurs, as the disease advances, the incidence of anxiety increases, and the incidence of major depression rises to between 23 and 58 percent. Anxiety and depression decrease the quality of life (Stark et al. 2002), but patients can often be treated effectively, even patients with very advanced disease.

Patients may experience anxiety in different degrees and patterns. Some present with panic disorders, general anxiety disorders, or phobias (Stark et al. 2002). Anxiety may manifest, for example, as uncontrolled worry, a sense of impending doom, motor tension, restlessness, autonomic hyperactivity (e.g., palpitations, sweating, dry mouth, tightness in the chest), nausea, vomiting, diarrhea, feeling on edge, difficulty concentrating or relaxing, insomnia, or irritability. Anxious people often feel out of control and helpless.

Some patients may experience anxiety only before each chemotherapy treatment or before hearing results of follow-up scans. Others are chronically anxious. Their anxiety may exacerbate, but they are never anxiety-free. Some patients with severe anxiety are actually suffering from a delirium. If, in addition to being anxious, the patient has hallucinations or extreme psychomotor agitation, or is disoriented or paranoid, the anxiety is likely to be part of a delirium and should be treated with the therapies described in Chapter 6.

Assessment of the *intermittently* anxious patient includes exploring what the patient thinks might be contributing to the anxiety, what makes it better, what makes it worse. Ask whether he uses alcohol or other drugs to ameliorate it. Don't stop the questioning until you feel fairly confident that you know what this patient is afraid of, or you know that you've gone as far as he'll allow in the questioning. Your inquiry may reveal, for example, painful memories of the suffering of a close family member or friend who had cancer many years ago, fears

of disfigurement, needle phobias, or claustrophobia, all of which may respond to directed interventions.

Finding a physiological cause for a patient's anxiety should not stop you from listening for additional psychological or spiritual problems that also cause anxiety. Mrs. Hanrahan was such a patient.

Curiosity, Not Certainty

Mrs. Hanrahan was a 59-year-old woman with extensive metastatic lung cancer that had been increasingly resistant to therapy. She worked for years as a superintendent of schools in a moderate-sized town and was married, with four children. We were asked to see her for shortness of breath and for the recent onset of episodes of rapid heartbeat that had occurred in the night during her summer vacation in Maine. She had practiced relaxation and yoga in the past but was unable to get her symptoms under control using these methods.

On initial questioning, we found that her dyspnea at rest was improved by increased oxygen but was still problematic with exercise. She was waking up at night with a sensation that her heart was pounding, and when that occurred, she increased the oxygen, to some effect. She also had these episodes during the daytime; they responded to lorazepam.

As I listened, I was thinking about how we could treat the dyspnea with more oxygen and the related anxiety with a different benzodiazepine, along with focused instruction to help her improve her use of yoga and relaxation techniques. But I suddenly realized that I really didn't know what had caused the anxiety. I had just assumed it was related to the pulmonary process. So I pursued the questioning a bit further.

Mrs. Hanrahan told me that during her vacation, she had decided to retire from her position and not return to school in the fall. She also said tearfully that several of her children were having a great deal of difficulty coping with her increasing debility.

As she talked and cried, with her husband comforting her, I realized how close I had come to missing the most important part of the story. She was suffering from so many new losses—her position at work, her independence, her roles as mother and wife. Freed from the administrative burden of her job, she could focus considerable attention on her declining health and her powerlessness to help her family. Clearly these were important contributors to her anxiety, and I would need other solutions if I were to have any chance to make it better.

As Mrs. Hanrahan explored with us these potential causes of her anxiety, I was able to help her identify the meaningful work that remained for her to do: with her loved ones, her students, and her colleagues. She realized she now had new goals,

purposes, and functions, and was able to reframe her roles, redefine her personhood, and begin to heal. We knew that enrolling in a hospice program would be helpful both for her and for her family (see Chapter 4), and she and her husband agreed. They understood that they would keep her oncologist, and if new, promising therapies appeared, he would let her know and she could disenroll. She went home having made an appointment with her yoga instructor and with a promise of support from hospice.

Evaluation of a *chronically* anxious patient also includes a thorough psychiatric history, seeking evidence of generalized anxiety, depression, social phobia, panic disorders, obsessive-compulsive disorder, or post-traumatic stress disorder. Also look for contributing medical causes, including cardiovascular, endocrine, metabolic, neurologic, and respiratory conditions.

ANXIETY: COMMON CONTRIBUTING MEDICAL CONDITIONS

- Cardiovascular: angina or infarction; arrhythmias; congestive heart failure; hypovolemia
- Endocrine: hypercalcemia or hypocalcemia; hypothyroidism or hyperthyroidism
- Metabolic: hyperkalemia; hypoglycemia; hypoxia; hyponatremia; fever
- Neurologic: akathisia; encephalopathy; partial complex seizure disorder
- Respiratory: asthma; chronic obstructive pulmonary disease (COPD); pneumothorax; pulmonary edema; pulmonary embolism
- Medications: glucocorticoids; antiemetics that cause akathisia (e.g., Compazine, Reglan); bronchodilators and beta-adrenergic agonists; stimulants (methylphenidate); antidepressants (e.g., fluoxetine, which also causes akathisia); caffeine; "rebound" from ultra-short-acting benzodiazepines (e.g., Xanax)
- Withdrawal syndromes: alcohol; benzodiazepines; opioids

(Adapted from Noyes et al. 1998, 555)

It is not uncommon for patients to be anxious only when they attend medical appointments, and the phenomenon of hypertension occurring only in that setting has been well described. But a more serious problem is an undisclosed history of *childhood sexual abuse* (Wygant et al. 2011). The 2006 WHO definition of childhood sexual abuse is "the involvement of a child in sexual activity that he or she does not fully comprehend, is unable to give informed consent to,

or for which the child is not developmentally prepared, or else that violates the laws or social taboos of society. Children can be sexually abused by both adults and other children who are, by virtue of their age or stage of development, in a position of responsibility, trust or power over the victim" (WHO 2006, p. 10). The actual prevalence childhood sexual abuse is unknown, but estimates are as high as one in three women and one in six men in the United States having a history of this abuse (Wygant et al. 2011). When a patient who has been abused has a diagnosis of cancer, even the physical examination can seem intensely intrusive, as can the testing involved, and the patient may have memories of the abuse or feel they are re-experiencing it. A history of childhood sexual abuse should be suspected in patients presenting with far-advanced cancers that are visible (such as breast cancers eroding the skin) as well as those who have a large number of unexplained symptoms; a substance abuse or alcoholism history; difficulty managing anger, anxiety, panic attacks, or claustrophobia; PTSD; difficulty trusting others; and problems getting along with numerous health care teams. A suggested screening question is: "Have you ever been touched in a manner that made you feel uncomfortable?" (Wygant et al. 2011). It is easy to see how someone with these concerns would be anxious at the time of physical examinations, or repeatedly miss appointments for staging examinations despite seeming to want to please the physician. A social worker or psychologist should, whenever possible, be part of the team caring for patients with suspected or confirmed childhood sexual abuse. Counseling, teaching self-comforting skills, and reinforcing that the patient is currently safe can help decrease anxiety.

Patients with anxiety respond to both nonpharmacologic and pharmacologic therapies. Counseling is discussed later in this chapter. Relaxation, hypnosis, and behavioral training also benefit patients with anxiety, and these are discussed in detail in Chapter 7. Pharmacologic therapies for anxiety (other than that associated with delirium) include benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), and atypical antipsychotics (e.g., quetiapine [Seroquel] and mirtazapine [Remeron]). The benzodiazepines are used to treat patients with mild anxiety (Table 9.1). Lorazepam (Ativan) (0.5 mg to 1 mg p.o. or sublingual t.i.d.) is recommended for intermittent anxiety. Clonazepam (Klonopin) (0.25 to 0.5 mg p.o. b.i.d., with 0.5 to 1 mg at bedtime) can be added for patients with chronic anxiety that is mild to moderate. In some patients, however, anxiety may unpredictably worsen in response to lorazepam. Alprazolam (Xanax) (0.25 to 2.0 mg p.o. t.i.d. to q.i.d.) is rapidly effective but has a "rebound" effect that causes a return of the anxiety in a short period. Oxazepam (Serax) (15 to 30 mg p.o. at bedtime), temazepam (Restoril) (7.5 to 30 mg p.o. at bedtime), or zolpidem (Ambien) (5 to 10 mg p.o. at bedtime) are often used to treat insomnia

due to anxiety. Clorazepate (Tranxene) (15 to 60 mg/day p.o.) is used for anxiety and acute alcohol withdrawal. Patients with more severe anxiety benefit from treatment with SSRIs (such as citalopram [Celexa] or escitalopram [Lexapro]) or with mirtazapine (Remeron) (see Table 9.1).

If the anxiety is due to drug-induced akathisia, discontinue the agent (e.g., metoclopramide, haloperidol) and start a beta blocker: oral propranolol (40 mg orally t.i.d.), or intravenous metoprolol at an equivalent dose (Avital et al. 2009). Zolmitriptan (7.5 mg p.o. daily) in a double-blind comparative study (Avital et al. 2009), and mirtazapine (15 mg p.o. daily), in a double-blind placebo- and propranolol-controlled trial (Poyurovsky et al. 2006) have also shown efficacy comparable to propranolol in reversing the akathisia, but patients in the Poyurovsky study were given only 40 to 80 mg of propranolol daily.

Depression

It can be difficult to discern which patients with advanced disease are depressed. Many of the usual somatic signs (e.g., anorexia, sleep disturbances, fatigue, or weight loss) are not helpful, because they may be due to the underlying illness. Depressed patients, however, will also feel sad, cry, be unable to get pleasure from any activity, or feel globally worthless, guilty, hopeless, or helpless.

PRACTICE POINTS: SIGNS OF DEPRESSION IN CANCER PATIENTS

- Appearing depressed or describing a feeling of depression
- Crying
- Inability to get pleasure from any activity
- Feelings of worthlessness, guilt, hopelessness, or helplessness

Note: Anorexia, sleep disturbances, weight loss, and fatigue occur in many patients with cancer; these signs do not identify those who are depressed.

Depression varies with the type of cancer a patient has. It is found in 33 to 50 percent of patients with pancreatic cancer, 22 to 57 percent of patients with oropharyneal cancer, 11 to 44 percent of those with lung cancer, and 1.5 to 46 percent of those with breast cancer (Massie 2004). Terminally ill patients who responded "Yes" to the screening question "Are you depressed?" were very likely to be confirmed as depressed in a more comprehensive evaluation. Useful follow-up questions include: How do you see your future? What do you imagine is ahead for you with this illness? What aspects of your life do you feel

most proud of? Most troubled by? Are you getting less enjoyment from your favorite things?

Depressive symptoms can be manifestations of any number of medical, social, spiritual, or psychiatric disorders. Common metabolic and medication-related causes of depression in cancer patients include hyponatremia, hypercalcemia, CNS tumor, high-dose interferon therapy, opioids, and corticosteroids. Stress from financial or family concerns or from simple sleep deprivation are also often contributory. If none of these is present, the patient may have either an adjustment disorder or, more rarely, a major depression.

Treatment of depression is often effective. As discussed in Chapter 5, care must be taken to optimize pain control in cancer patients, because uncontrolled pain is a major risk factor for depression and for suicide. Psychological strategies include psychopharmacology and psychotherapy.

There are several agents that are often effective in alleviating depression. The most rapidly acting antidepressants are the psychostimulants dextroamphetamine and methylphenidate (2.5 to 5 mg at 8 a.m. and noon, maximum 60 mg), which often act within a few days. The selective serotonin reuptake inhibitors (SSRIs) or the serotonin and norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine and duloxetine, are the first choice when immediate onset is not needed; they may take 4 to 6 weeks to show effect. Initial doses are usually small. They are given for 3 to 7 days and then increased every week or every other week until the patient notices a benefit or the maximum dose is reached. If the patient is expected to live longer than a few months, a stimulant and an SSRI or an SNRI may be started simultaneously, and the stimulant can be titrated off 4 weeks later.

The SSRIs and SNRIs can be directly substituted for one another without cross-tapering (Howard et al. 2012), but they should not be stopped suddenly; they should be tapered if they are to be discontinued. If a patient develops a bowel obstruction or mucositis or for some other reason is unable to take oral medications, and you have not had the opportunity to taper the antidepressant, your patient may complain of a flu-like syndrome, insomnia with vivid dreams, nausea, ataxia, paresthesias, and anxiety or agitation. You may need to use a lorazepam taper to treat the anxiety that is likely to occur within days if the patient is on paroxetine (Howard et al. 2012), or up to a week later if the patient was taking one of the other agents.

Suggested Initial and Maximal Doses for SSRIs

- Citalopram (Celexa): 10 mg/day orally for the first week. If no response, increase by 10 mg weekly to the maximum dose of 60 mg/day. Doses

greater than 40 mg of citalopram have been associated with a prolonged QTc, so if the higher doses are needed, check an EKG and minimize other drugs that prolong the QTc (e.g., levofloxacin, metoclopramide, methadone).
- Escitalopram (Lexapro): 5 mg/day orally for the first week, then increase to the maximum dose of 20 mg/day. High doses of escitalopram have been associated with a prolonged QTc, so if the higher doses are needed, check an EKG and minimize other drugs that prolong the QTc (e.g., levofloxacin, metoclopramide, methadone).
- Fluoxetine (Prozac): 5 to 10 mg/day orally for the first week; increase by 10 mg every 2 weeks to the maximum dose of 80 mg/day, as it has a long half-life.
- Fluvoxamine (Luvox): 25 mg at bedtime for the first week; increase to the maximum dose of 200 mg/day as needed.
- Sertraline (Zoloft): 12.5 to 25 mg/day in the morning for the first week, then increase to 50 mg for an additional week. Increase as needed by 25 mg to the maximum dose of 200 mg/day.
- Paroxetine (Paxil): 10 mg orally at bedtime; increase to a maximum of 40 mg/day as needed.

Suggested Initial and Maximal Doses for SNRIs
- Duloxetine (Cymbalta): 10 to 20 mg orally in the morning or twice a day; increase as needed to a maximum dose of 20 to 60 mg once or twice daily.
- Venlafaxine (Effexor): 18.75 to 37.5 mg orally twice a day for the first week; increase by 75 mg per week to a maximum dose of 150 mg twice a day. Missing any dose of venlafaxine can cause symptoms similar to those experienced with opioid withdrawal, so the patient must be weaned off the drug carefully.
- Venlafaxine extended release (Effexor XR or venlafaxine ER): 37.5 mg orally every morning or twice a day for the first week; increase by 75 mg per week to a maximum dose of 100 mg twice a day.

The mechanism of action of the antidepressant mirtazapine (Remeron) (7.5 to 15 mg orally or sublingually at bedtime, to a maximum of 60 mg/day p.o.) is unknown; it does bind central alpha-2, 5-HT2, and 5-HT3 receptors, and in addition to its antidepressant actions, it is useful for insomnia, as it is sedating, and it enhances appetite. Mirtazapine (15 mg) can be directly substituted for an SSRI (e.g., fluoxetine 20 mg, citalopram 20 mg) (Howard et al. 2012). Buproprion is an aminoketone used both for smoking cessation (as Buspar) and for patients with depression (as Wellbutrin) (100 mg p.o. b.i.d. to a maximum of 450 mg given

in four divided doses, or bupropion XL 100 mg daily, increasing to a maximum of 200 mg p.o. b.i.d.). It is "activating" and particularly helpful for patients with retarded psychomotor function, in whom anxiety is not a major problem. QTc prolongation was seen in a case of massive overdose, but not otherwise (Goodnick et al. 2002). Trazodone (Desyrel) is also sedating. Initial doses are 50 mg orally at bedtime, to a maximum of 400 mg/day. Trazodone may prolong the QTc. Tricyclic antidepressants (e.g., amitriptyline, nortriptyline, desipramine, doxepin, imipramine) are less useful for patients with advanced disease, because of their side-effect profile. But if the patient also has neuropathic pain, you can try to enhance tolerance of the drugs by starting at very low doses (10 mg at bedtime) and increasing by 10 to 20 mg weekly. If there is no effect, check blood levels to ensure that the therapeutic range has been reached. Checking EKGs to detect conduction disturbances, including prolonged QTc, may be necessary when giving higher doses.

Choice of agent. Side effects and drug-drug interactions both influence the choice of antidepressant. Major side effects of the SSRIs and SNRIs include hyponatremia, sexual dysfunction or loss of libido, somnolence, and gastrointestinal complaints (e.g., nausea, diarrhea, vomiting, and foul-smelling flatus). Citalopram, escitalopram, venlafaxine, duloxetine, and mirtazapine are the least likely to have drug-drug interactions; sertraline is likely, and fluoxetine, fluvoxamine, paroxetine, and all the tricyclic antidepressants are very likely to interact with other drugs cancer patients are taking. Rarely, patients can develop serotonin syndrome when other agents are added, like fluconazole, that inhibit the metabolism of the SSRIs (i.e., inhibitors of CYP2C19 and 3A4), which causes a marked increase in SSRI blood levels (Levin et al. 2008). I discuss serotonin syndrome under the Delirium section of Chapter 6.

If the patient does not respond to first-line agents, a psychiatrist should be consulted. Referral to a psychiatrist is also necessary in any of the following situations: the physician is unsure of the diagnosis; the patient is psychotic, confused, or delirious; the patient previously had a major psychiatric disorder; there are dysfunctional family dynamics; or the patient is suicidal or is requesting assisted suicide.

Factors that make cancer patients more likely to attempt suicide include advanced illness and poor prognosis; uncontrolled pain; depression and hopelessness; delirium and disinhibition; loss of control and helplessness; preexisting psychopathology; prior history of attempted suicide and family history of suicide; and exhaustion and fatigue. Patients with pancreatic cancer are eleven times more likely to commit suicide than the people in the general population and are at particular risk in the early postoperative period (Turaga et al. 2011). The psy-

chiatrist will not necessarily advise hospitalization if the patient's physical condition makes that inadvisable; the psychiatrist will, however, help the home care agency and the family take appropriate precautions.

Personality Disorders

Oncologists frequently find themselves trying to care for patients who don't clearly have an anxiety disorder or depression, who are not delirious, but who stress the team to the maximum. Patients like Duane, who one minute, is praising you to the skies, and the next, is outraged and threatening you when you won't refill an opioid prescription to replace one that was accidently left in his motel room on vacation. Or Susanna, who, despite long discussions in the office, calls repeatedly to ask for help deciding the most trivial concerns. Or Arthur, who misses appointments, doesn't follow instructions regarding medications, and repeatedly calls all members of your staff seeking support and problem solving but rarely follows through. How can you understand what is causing this behavior, and who can help you and your staff manage these patients? How can you treat these people safely with chemotherapy or opioids?

I was relieved to learn that patients like these, "difficult" patients, have clearly described personality disorders. Patients with personality disorders have been studied extensively, and learning about them, how they see the world, and what they expect from us has made a confusing and exasperating situation into a problem our team can manage. I now understand better how to create effective boundaries that will make them feel safer, and how to moderate the chaos they bring to my staff or the inpatient care team.

Drs. Meyer and Block, in their review "Personality Disorders in the Oncology Setting" (2011), clarify for us what makes taking care of patients like these a "difficult encounter." In their extremely useful paper, they describe how these patients present, their behaviors with the oncology team, our possible reactions to them, how we can respond to them, what medications might be helpful, and even what we can say in response to the challenges they present us with.

Types of personality disorders. Meyer and Block list seven personality disorders that are particularly problematic in medical settings: paranoid, antisocial, narcissistic, borderline, histrionic, dependent, and obsessive-compulsive.

Duane is antisocial. He initially seems charming, but he is really manipulative, and you may find that he has fired other providers, or has found himself on the wrong side of the law. Our reaction to him may be "sympathy, followed by anger and fear," and the best strategy for dealing with him is to acknowledge your feelings and set limits on his behavior to protect yourself and the staff. If

you need to treat his anxiety, don't use benzodiazepines, which he may easily divert; use an SSRI.

Susanna is "dependent," and your reaction to her is likely to be fatigue, then guilt for not taking her calls, and finally aversion. Again, acknowledge your feelings, set limits, then reassure her that you're committed to her care, but let her know the recurrent calls to your staff for non-emergencies are making it harder for them to take care of her. Her anxiety may respond to SSRIs or low-dose benzodiazepines.

Arthur is narcissistic, and although he behaves well when everything is going OK, he can be very angry and expect special treatment from you, demanding you be there for him whenever he needs you. You may in turn become angry at him and wish to attack back. Meyer and Block suggest we "not challenge the entitlement, but channel it into partnership in providing the best care; emphasize and align with patient strengths." If patients like Arthur are depressed, or have mood lability, then SSRIs for the depression, or mood stabilizers or antipsychotics, are recommended.

The most disruptive disorder in the clinical setting is likely to be the "borderline" patient. This is someone everyone in the office knows about and has tried to help at one time or another. She may have fired several previous doctors and nurses. When she is admitted, the nursing staff may be up in arms, and social work, patient relations, even security may be involved. These patients are impulsive, emotionally labile, and afraid that we will abandon them. Their impulsivity may manifest as aberrant drug use, being sexually promiscuous, or missing appointments and medication doses. They feel especially uneasy during transitions, such as discharge from the hospital, or completion of adjuvant chemotherapy, and are likely to present with new symptoms or problems.

These "borderline" patients need a team that is empathetic but has low expectations, one in which all the caregivers must meet as frequently as necessary, even daily, to ensure they are on the same page. Team members or office staff must be alert to the possibility that the patient may try to turn staff against each other because of how the patient perceives she has been treated. Psychiatrists should be part of these teams whenever possible. Limits must be set and clearly stated and restated, along with ongoing reassurance that the oncology team is committed to care for the patient. The patient must be told, even though the reaction may be anger or outrage, that chemotherapy and opioids require regularity of visits and collaboration with the plan of care. If the patient is depressed or anxious, SSRIs can be helpful, along with atypical antipsychotics for anger or impulsive behavior. Patients given opioids must be monitored

very closely, and benzodiazepines should be avoided because of their abuse potential.

I hope that after reading this section, you are saying to yourself, "Oh, that was what was going on with Mr. X!" or "That really describes Mrs. Y!" Once you learn to recognize these patients early in your relationship with them, you will find it useful to discuss with your staff the patient's sense of what is going on, what the patient likely needs for support, who on the team are able to give that support, and what the boundaries should be. You can make a plan for each office visit or admission delineating who will be the "point person" caring for this patient, who will support that person in that role, and when to pre-meet and debrief about patient encounters. It sounds like a lot of work, and it is, but without it, the staff is likely to be continually disrupted as long as the patient is in the practice or on the inpatient unit. With appropriate teamwork and boundary setting, these patients may be able to receive the care they need from the team safely and consistently.

Counseling

Psychological therapy. Social workers, psychologists, and psychiatrists are equipped with an array of cognitive techniques that can help the patient and family lessen their distress. These clinicians can offer support and education and can help in developing coping skills. They can diminish patients' anxiety, depression, or delirium, any of which may exacerbate pain.

Psychiatric therapy can be offered to the patient (either individually or in a group) or to the family or significant friends. Groups can be particularly helpful for cancer patients because of the similarities of the psychological problems posed by the disease in its various stages. Those who have passed through one or another stage can share their successes with others now facing the same problems. By becoming teachers, patients and their families can increase their own sense of self-worth.

In addition to the strategies useful for clients who do not have or have never had cancer, there is now a large body of information on the specific psychological needs of cancer patients. Work has been done on the implications of a wide variety of cancer-related practices, from genetic testing and cancer screening to the psychological, social, and behavioral factors that influence the risk of cancer and the nature of survival from it. Information is available on the needs of cancer survivors, patients with specific cancers (e.g., lung cancer, breast cancer) and their families, and patients receiving specialized therapies (e.g., bone marrow transplants), as well as on the pharmacologic and nonpharmacologic

interventions appropriate for them. Much is also known about the psychological stresses experienced by both the families and the professional caregivers of patients with cancer.

The new field of psycho-oncology is responsible for this wealth of information and research-based recommendations for care. A comprehensive overview of the breadth and depth of the field is found in the second edition of the textbook *Psycho-oncology*, edited by one of its pioneering practitioners and researchers, Dr. Jimmie Holland. As she states in the book's preface, "This present volume describes the many ways in which mental health professionals have indeed contributed to improving the lot of the cancer patient." A thorough discussion of psycho-oncology is beyond my expertise, but I refer those who are interested to this fascinating text. I discuss below the role of psychiatrists and counselors in the care of cancer patients.

PRACTICE POINTS: THE ROLE OF PSYCHIATRISTS AND COUNSELORS IN THE CARE OF CANCER PATIENTS

- Therapists provide psychological and emotional support and education about cancer and its treatment(s); they teach coping skills.
- Therapists facilitate communication of the patient's and family's concerns to and among health care providers.
- Therapists evaluate and address the psychological needs of the family.
- Therapists recognize and treat adjustment disorders, anxiety, depression, and delirium.

Support. Using a crisis intervention model, therapists can support cancer patients by providing emotional support and by being there for them throughout the disease process. Patients with cancer need continuity but instead usually see a number of specialists during the process of diagnosis and treatment—the general internist, radiologist, and medical, surgical, or radiation oncologist. The therapist can provide the needed continuity and, when necessary, can be the spokesperson for the family and patient if they are unable to explain their needs to whichever oncologist is currently treating the patient.

Education. The therapist can also provide information about the disease and help the patient gain useful self-knowledge. Therapists who work with cancer patients are usually well informed about the disease and its treatment, and patients may find it easier to ask them the questions they are reluctant to "bother" their oncologist with. Therapists can also help dispel misconceptions, such as

those about taking pain medications, discussed in Chapter 2. They can clarify therapeutic goals and reinforce the legitimacy of reporting treatment-related side effects if they arise.

But therapists also anticipate the emotional and psychological stresses that patients are likely to face and can help them prepare by rediscovering coping strategies that have served them well in the past. Cancer is rarely the first major crisis a person has faced. The first may have been something as simple as passing an important examination or as complex as being in a front-line unit in combat. Therapists can help patients recall a crisis that they managed successfully and then, along with the patient, analyze the strategies that worked and decide how to apply the same techniques to the current crisis: being a cancer patient.

Skill development. The task of helping patients develop new skills also puts therapists in the role of teacher, as they instruct patients in relaxation and other cognitive coping techniques. The therapist can also teach patients another skill that is crucial to obtaining the best care during their illness: how to explain their needs to health care professionals.

Patients are unaccustomed to being assertive with physicians or nurses; but they may need to assert themselves if they are to retain their rights as people, even as they are being forced to take on the role of patient. In hospital settings, common courtesy is often forgotten even when no medical emergency has supervened. There is no reason, for example, that a person has to stop eating breakfast because it is convenient for a house officer or a phlebotomist to draw a blood sample at that moment. If the timing is important, the patient is owed both an explanation and an apology for the inconvenience.

There is also no need for a patient to suffer because she is afraid to tell the physician that the pain regimen isn't working. Therapists can help patients feel comfortable relinquishing this Good Patient role. Not only will the patient then be able to retain her sense of control and self-esteem even in the hospital setting, but she is much more likely to share all her concerns with us and frankly inform us if our symptom-oriented therapies are not working.

Treatment of related psychiatric disorders: anxiety, depression, and delirium. Psychotherapy for anxiety and depression is often as effective as pharmacologic therapies; it can be combined with them and, in selected patients, can substitute for them. And counseling can help unravel complicated relationships that are causing distress to patients and their families. It is often difficult for patients and their families to realize that they would benefit from psychiatric or psychological help (Breitbart et al. 2010). They might misinterpret your offer of a referral as indicating that you think they are "crazy." I often need to spend a little time explaining why I think patients and families need the referral and

how, specifically, I expect the therapist to help them. The Abernathy family benefited significantly from the counseling they received.

The Benefits of Psychological Counseling

John and Mary Abernathy were the parents of my patient Patricia, a 26-year-old woman with extensive, refractory sarcoma. Patricia required large doses of opioids along with adjuvants for her pain, but she felt that the pain was well controlled, and she enjoyed going to movies and sports events with friends as her energy level allowed. Over several months, despite satisfactory pain control, the hospice nurses noted a gradual change in Patricia, which I confirmed on a visit to her parents' home, where she lived.

Patricia looked very sad, was eating less, and told me that even when she felt up to it, she had no desire to see friends or go out with them as before. Her mother brought in a tray with her lunch and after she left, Patricia dissolved in tears. She said she was feeling terribly guilty for being such a burden to her family, that she could not contribute a thing to the running of the household, and that she was just of no use to anyone. She did not want to end her life herself, but she didn't think it was really worth living anymore. She asked that I not tell her parents how she felt because that would just distress them further.

After I left her room, Patricia's parents also shared their concerns with me. They had noticed the change in their daughter but had ascribed it to "all the dope" I had prescribed for her pain. They didn't want to let Patricia know how upset they were about her changed condition, but they wanted something done to alleviate her distress.

Before leaving that day, I spoke with Patricia and her parents about the differences in their perceptions and the communication difficulties they were having. I told everyone that I thought Patricia was depressed, that depression commonly affected patients whose cancer was as far advanced as Patricia's, but that I had every hope that the depression would respond to treatment. I suggested that in addition to individual therapy for Patricia, family therapy might help them understand each other's concerns and improve their ability to share them, and they agreed to try it.

The therapist later informed me that Patricia improved considerably, as did communication within her family. The therapist continued to provide support and counseling until Patricia's death, and she helped Patricia's parents cope with their bereavement.

If you're able to convince your patients and their families to accept this type of help, you will have opened the door to a complementary therapeutic experience for them. In their relationship with the therapist, they can ventilate and

explore their feelings toward the cancer without expressing any "unacceptable" doubts to you, to your staff, or to other family members.

With careful preparation, many patients will at least explore the possibility and accept the referral without feeling either betrayed or rejected by you. While you are focusing on the medical care, the social worker or other therapist can identify psychological or social problems that otherwise might never come to your attention and yet would be sources of distress for your patients and their families. And as part of a hospice team, therapists are often available 24 hours a day and can be helpful in emergencies.

Oral Problems

Many simple measures can help patients maintain oral comfort. These include removing poorly fitting dentures; replacing vitamins and minerals that, if deficient, can result in mucositis (e.g., vitamins B, C; zinc); presenting food at moderate temperatures; avoiding dry, acidic, or highly spiced foods; and minimizing alcohol and tobacco use.

PRACTICE POINTS: MAINTAINING ORAL COMFORT

- Remove poorly fitting dentures.
- Correct vitamin and mineral deficiencies.
- Present foods at moderate temperatures.
- Avoid dry, acidic, or highly spiced foods.
- Minimize alcohol and tobacco use.
- Continue routine prophylactic oral care, including brushing, flossing, and rinsing with an alcohol-free antibacterial mouthwash.
- Monitor for oral candidiasis and treat early.

Oral comfort can also be maximized by continuing routine prophylactic oral care, even for patients who are very debilitated (Table 9.2). Regular mouth care can be carried out by the patient or the family; it can help stimulate the patient's appetite and diminish discomfort from various causes. Patients should be encouraged to continue brushing daily using a soft-bristle brush, flossing, and rinsing with an antibacterial mouthwash (that does not contain alcohol) or a solution of bicarbonate in water (e.g., 1 tsp. in a cup of water). More detailed oral care protocols are described in sources listed in the bibliography at the end of the chapter.

Despite these preventive regimens, about half of cancer patients will develop oral discomfort, the most common causes of which are candida infections; treatment-induced mucositis; or xerostomia resulting from mouth breathing, previous radiation therapy, or medications for pain or other symptoms. Simple methods of treatment are often effective.

Candida

Etiology. As many as 90 percent of cancer patients have contracted an oral candida infection by the time they die. About 50 percent are colonized before chemotherapy, but more than 70 percent are colonized after chemotherapy or radiation therapy, and almost 40 percent of patients receiving radiation therapy to the head and neck or on chemotherapy have clinical oral fungal infections (Lalla et al. 2010). Oral and esophageal infection with candida can also arise in patients who have recently been on a course of antibiotics, which alter the normal protective oral flora. Other patients are predisposed to developing yeast infections due to immunosuppression resulting from therapeutic steroid doses or malnutrition (albumin of <3 g/dL).

Manifestations in immunosuppressed patients. Oral thrush presents most often as a burning tongue and pain when eating. Examination of the oral cavity may reveal only a beefy red tongue (in those who have recently been taking antibiotics) or white plaques (which are easily wiped off, but with bleeding) along the sides of the tongue or cheeks, on the gums, or on the roof of the mouth. Patients who leave their dentures in place between meals are particularly prone to develop both angular cheilitis and candidal infections on the roof or floor of the mouth; these appear as red edematous areas.

Candidal esophagitis can contribute to anorexia by causing dysphagia. The lower esophageal sphincter area is most commonly involved, but the pain or the sensation of food "sticking" can be present in the throat or chest as well as in the upper abdomen. Topical antifungal medications that are effective for oral thrush unfortunately do not prevent esophageal candida infections.

Therapy. Topical agents (e.g., clotrimazole troches or nystatin suspensions) are recommended and usually tried first, but for various reasons, they are often not effective in this population (Lalla et al. 2010). The troches do not dissolve when patients have concurrent xerostomia, for example. Moreover, swishing a suspension of nystatin, which tastes terrible, four or five times a day, or taking troches that dissolve in the mouth every 5 or 6 hours is inconvenient for a patient with advanced cancer. Fluconazole, on the other hand (200 mg loading dose followed by 100 mg p.o. / day), provides effective prophylaxis and therapy

for these patients (Lalla et al. 2010). Itraconazole (100 to 200 mg tablets or oral suspension daily) and amphotericin B 100 mg/ml oral solution (1 ml t.i.d. to q.i.d.—swish and spit out) are also effective.

Herpes Simplex Virus

Oral HSV infections commonly cause morbidity in patients with hematologic malignancies as well as in as many as 50 percent of patients with head and neck cancer treated with chemo- and radiation therapy (Elad et al. 2010). Patients who about to undergo transplant or leukemia therapy routinely receive antiviral prophylaxis with acyclovir or valacyclovir to prevent reactivation, and both are equally effective in preventing HSV reactivation (Elad et al. 2010).

Treatment-Induced Mucositis

Treatment-induced mucositis is one of the most common and most distressing side effects from chemotherapy and radiotherapy and from bone marrow transplants. Patients generally treat this with an intensive regimen of oral cleansing with frequent saline and antiseptic rinses daily. The following have all been used: amifostine (a free-radical scavenger) and benzydamine hydrochloride; antimicrobials (which attenuate pro-inflammatory cytokines); l-glutamine (which replaces l-glutamine losses); granulocyte-monocyte colony-stimulating factors; and superoxide dismutase inhibitors (Sonis 2004).

Recombinant human keratinocyte growth factor (rHu-KGF; palifermin from Amgen), improves soreness and ability to eat, drink, sleep, and talk for patients receiving high-dose chemotherapy and total body irradiation (TBI) as part of a bone marrow transplant procedure (Peterson and Cariello 2004).

Xerostomia

Etiology. Dry mouth is a very common complaint of patients with far-advanced cancer. Some have received radiation that has diminished their saliva production, and others are taking medication that is causing xerostomia as a side effect. Therapy is often effective in these patients and in those without a clear underlying cause.

I find it useful to review the patient's medications to see which could be contributing, and then discontinue these and if necessary substitute other agents that are less likely to induce this side effect. In addition to the antihistamines and anticholinergics, certain anticonvulsants, antipsychotics, hypnotics,

PRACTICE POINTS: THERAPY FOR XEROSTOMIA

- Minimize the number of medications that produce xerostomia.
- Try sugar-free sour lemon drops or other sugar-free hard candy.
- Encourage continued good routine oral hygiene, adding a fluoride-containing toothpaste for selected patients.
- Try pilocarpine (Salagen), bethanechol, or cevimeline (Evoxac) to ameliorate radiation-induced xerostomia.
- Acupuncture can improve salivary flow.

beta-blockers, morphine, and diuretics can contribute to xerostomia. The more of these agents the patient is receiving, the more likely he is to develop xerostomia.

Cancer therapy also induces xerostomia (Jensen et al. 2010a, 2010b). Patients who receive conventional, 3D-conformal, or intensity-modulated radiation therapy that includes the parotid, submandibular, and minor salivary glands all develop some degree of permanent xerostomia. Patients who are candidates for intensity-modulated radiation therapy (IMRT) that spares the parotid, however, less often develop salivary dysfunction, and the xerostomia is less severe (Jensen et al. 2010a). Many of these patients gradually recover full salivary secretion over one or two years. Xerostomia caused by conditioning total body irradiation and chemotherapy for hematopoietic stem cell transplantation, or other forms of chemotherapy or immunotherapy, is also usually transient (Jensen et al. 2010a).

Therapy. Sugar-free sour lemon drops or other sugar-free acidic hard candies are useful for patients with mild xerostomia (Jensen et al. 2010b). To prevent mouth pain and protect the teeth, I ask patients to avoid foods that contain sugar and encourage them to continue routine oral hygiene, supplemented, in some patients, with fluoride rinses.

Using IMRT to spare the salivary glands whenever possible, as mentioned above, minimizes the incidence and severity of xerostomia, and the xerostomia is usually only transient (Jensen et al. 2010a). Amifostine is a radioprotectant and free-radical scavenger that diminishes the toxicity of radiation to normal tissues. Its efficacy was shown in phase III studies, but there is still controversy about its use. Subcutaneous infusion avoids the hypotension and allergic reactions related to intravenous infusion, but patients still experience nausea and vomiting (Jensen et al. 2010b).

For those without cardiac contraindications, the muscarinic agent pilocarpine (Salagen) (5 to 10 mg t.i.d.) an hour before meals has been shown in ran-

domized controlled clinical trials to be effective in inducing saliva production in patients who have undergone radiation to the oral cavity or neck (Jensen et al. 2010b). The cholinergic agonists cevimeline (Evoxac) (30 mg p.o. t.i.d.) and bethanechol, both of which work through muscarinic receptors, are also effective (Jensen et al. 2010b).

Acupuncture (but not sham acupuncture) increases salivary flow and reduces xerostomia-induced problems, and with follow-up therapy, the effects have been reported to last as long as three years (Blom and Lundeberg 2000). Mucosal lubricants and saliva substitutes can be used by patients who do not respond to any of these therapies.

Gastrointestinal Problems

Ascites

Ascites is most common in patients with ovarian or breast cancer but also occurs in those with other genitourinary and gastrointestinal cancers and even in some with cancer of the lung. Ascites that is refractory to the usual diuretic measures (Aldactone [spironolactone] ± oral furosemide) can be difficult to manage. Adding oral hydrochlorothiazide or discontinuing oral furosemide and substituting intravenous furosemide infusions (100 mg over 24 hours) or Bumex (bumetanide) (0.5 to 2 mg/day p.o. or 0.5 to 1 mg IV—do not exceed 10 mg/day) may be effective. For other patients, not until their disease advances and their oral fluid intake diminishes does the ascites stabilize or decrease.

Peritoneovenous shunts. If patients have only a few months to live, repeated paracentesis may be the most appropriate therapy. Patients who need frequent paracentesis often have a Port-a-Cath or PleurX catheter placed in the abdominal wall to facilitate the repeated taps.

But for those patients with a reasonable life expectancy for whom ascites is a major problem, consider a surgical referral for percutaneous insertion of a peritoneovenous shunt (i.e., a Denver shunt or a LeVeen shunt) under local anesthesia in the operating room. These shunts were originally designed for patients with cirrhosis but have been useful in some patients with malignant ascites, particularly those with metastatic breast or ovarian cancer, who live a relatively long time.

The Denver ascites shunt combines a venous catheter, a compressible pump with one-way valve(s), and a catheter that is placed into the ascites (Figure 9.1a). The portions of the catheters not in a vein or in the ascitic fluid are tunneled subcutaneously, and the pump is also placed subcutaneously over ribs, to make it easier to compress (Figure 9.1b).

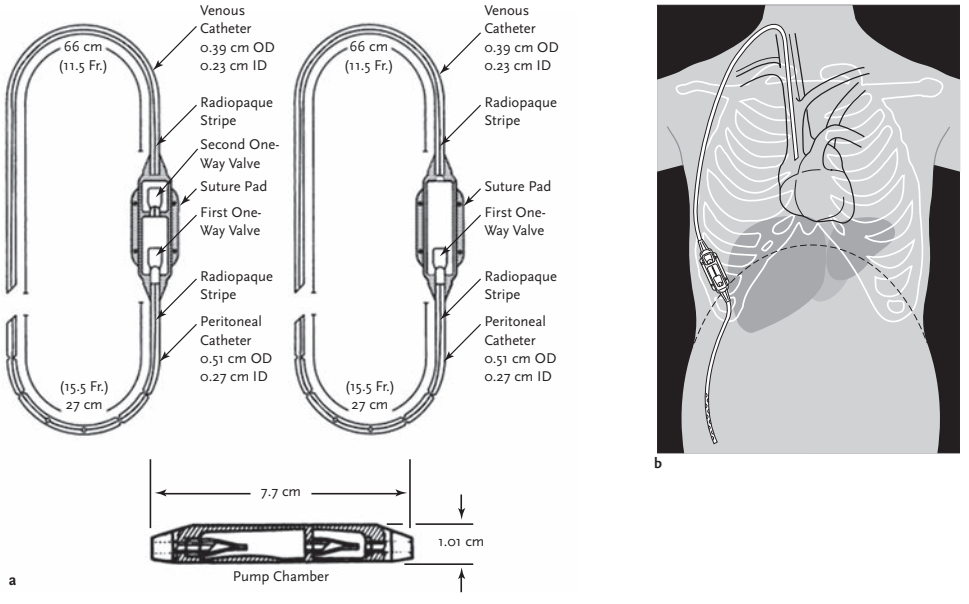

Figure 9.1. (a) Peritoneovenous shunts and (b) shunt placement. Courtesy of CareFusion Corporation or one of its subsidiaries, 2010. All rights reserved.

In response to the negative intrathoracic pressure induced by inspiration, ascitic fluid drains into the central venous circulation either through the one-way valve (the LeVeen shunt) or through a compressible valve system containing either a single- or double-valved shunt, depending on the viscosity of the ascites (the Denver shunt). Even more ascitic fluid can be moved into the central venous system if the patient uses an incentive spirometer.

For about 70 percent of patients with a Denver shunt, their ascites is resolved until death. The major complication, found to occur in about 25 to 30 percent of patients several months after shunt insertion, is reaccumulation of ascitic fluid due to obstruction of the one-way valve by the high protein content of malignant ascitic fluid. Other complications, found in fewer than 10 percent of patients, include pulmonary edema responsive to diuretics and ascitic leaks, which stopped spontaneously. Fewer than 5 percent develop clinically significant disseminated intravascular coagulation, shunt infection (which required shunt removal), or superior vena cava occlusion (Faught et al. 1995). Cancer cell implants may occur at the venous anastomotic site, but they will not cause the shunt to fail or hasten the patient's death.

A surgical option for relief of ascites due to portal or hepatic vein obstruction (not peritoneal carcinomatosis) is a transjugular intrahepatic portosystemic shunt

(TIPS). These shunts are used mainly for patients with ascites from hepatic failure due to cirrhosis, but they have been effective for patients with malignant ascites.

Diarrhea

Etiology. Diarrhea is less common than constipation or nausea and vomiting, but it is found in 4 to 10 percent of terminally ill cancer patients. Common cancer-related etiologies include newly acquired lactose intolerance (e.g., after chemotherapy); chemotherapy-induced gastrointestinal toxicity, especially prominent with 5-fluoruracil and its related agents as well as irinotecan; drug effects (metoclopramide or excessive laxatives) or side effects (caffeine, theophylline, antibiotics); intermittent bowel obstruction; fecal impaction; sphincter incompetence (e.g., due to rectal cancer or spinal cord lesions); chronic radiation enteritis; infection; graft-versus-host disease; or products of neuroendocrine tumors. Small cell lung cancers, for example, can produce vasoactive intestinal peptide (VIP), calcitonin, or gastrin. These and other substances from rarer tumors, such as gastrinomas, pheochromocytomas, medullary carcinoma of the thyroid, and especially malignant carcinoid, can cause voluminous diarrhea.

Therapy. Specific treatment for the conditions noted above is often effective. Treatment for the diarrhea related to graft-versus-host disease (GVHD) includes resting the gut by making the patient NPO, using antimotility agents, judiciously using opioids for abdominal cramping, and taking small doses of octreotide with care being taken not to induce an ileus. IV octreotide 500 mcg every 8 hours for seven days is given (Ippoliti et al. 1997). Evidence defining the optimal antidiarrheal therapy or nutritional support for these patients is not yet available (Kornblau et al. 2000; van der Meij et al. 2012).

Even the diarrhea caused by the serotonin and substance P secreted by carcinoids is often controllable with octreotide (150 to 300 μg SQ b.i.d. or over 24 hours by continuous infusion). The use of simple subcutaneous pumps, or instruction of family members in the technique of subcutaneous injections, enables patients to be successfully treated at home. Carcinoid-induced diarrhea may also respond to cyproheptadine.

When specific treatment is unavailable or is ineffective, patients can still be treated symptomatically. Rehydrate them orally using a solution of salted, sugared water such as Gatorade, or intravenously if necessary, and instruct the patient to avoid fats and milk products until the diarrhea resolves. For the diarrhea itself, use loperamide (Imodium), 4 mg initially, then 2 mg after each loose stool, to a maximum of 16 mg / 24 hours. If this is ineffective, try tincture of opium, 15 to 20 drops orally every 4 hours.

Dysphagia, Nausea, and Vomiting

Etiology. Dysphagia, nausea, and vomiting are often amenable to therapy in patients with cancer, even when the cause is irreversible. Dysphagia can be induced by esophageal candidiasis, as mentioned above; by cancer of the head and neck or of the esophagus; or by the chemotherapy and radiotherapy used to treat it. If the cancer responds to therapy, the dysphagia will usually resolve or at least improve. Patients with unresectable esophageal cancer can achieve significant reduction of their dysphagia from short courses of chemo/radiotherapy (Hayter et al. 2000). For sicker patients, single-dose brachytherapy was found to be as good as esophageal stenting in relieving dysphagia (Homs et al. 2004).

PRACTICE POINTS: NONPHARMACOLOGIC THERAPY FOR PATIENTS WITH NAUSEA

- Provide frequent, small feedings of cold foods.
- Remove foods with unpleasant smell or visual appearance, even if they were prepared for other family members.
- Serve meals in pleasant, comfortable surroundings.
- Refer the patient for progressive relaxation training, hypnosis, or acupuncture.

Causes of nausea and vomiting include chemotherapy and radiation therapy, disorders of the eighth nerve or vestibular apparatus, constipation, opioids, anxiety, disease of the CNS, hepatic or renal failure, gastritis or gastric ulcer disease, gastric outlet or bowel obstruction, hyponatremia, or hypercalcemia.

Therapy. Reversal of the underlying causes, whenever possible, is recommended. Constipation is a particularly common cause of nausea that can be overlooked, because patients assume they should not have many bowel movements if they are not eating as much. Management of constipation, including that induced by opioids, is reviewed in Chapter 6. For patients with other underlying causes, both nonpharmacologic and pharmacologic methods can be employed.

Families can provide frequent, small feedings of cold foods (which have less odor than warm foods) and remove foods whose sight or smell is unpleasant for the patient. Acupuncture, hypnosis, and progressive relaxation techniques have all shown some effectiveness, especially when the cause is anxiety.

Therapy can often be customized to treat the cause of the nausea (Table 9.3). Prochlorperazine (Compazine) and ondansetron (Zofran) prevent nausea that

commonly occurs during the first few days of opioid therapy. Hyoscyamine (Levsin), scopolamine (Transderm Scōp), or meclizine (Bonine, Antivert) are very helpful for patients with persistent nausea due to opioids or noninfectious inner ear problems; patients with these problems describe symptoms of motion sickness or may complain that the room is spinning (LeGrand and Walsh 2010). For nausea caused by gastric irritation from excess acid, a proton pump inhibitor (e.g., esomeprazole 20 mg p.o. daily or b.i.d.) or an H2 blocker (e.g., famotidine 300 mg b.i.d.) will help. For gastroparesis not due to opioids, metoclopramide is effective orally (5 to 10 mg b.i.d. to q.i.d.) or by continuous subcutaneous or intravenous infusion (1 to 3 mg/hr). If patients develop akathisia from metoclopramide, discontinue it and start a beta blocker: oral propranolol (40 mg orally t.i.d.) or intravenous metoprolol at an equivalent dose (Avital et al. 2009). Zolmitriptan (7.5 mg p.o. daily) in a double-blind comparative study (Avital et al. 2009), and mirtazapine (15 mg p.o. daily), in a double-blind placebo- and propranolol-controlled trial (Poyurovsky 2006) have also shown efficacy comparable to propranolol in reversing the akathisia, but patients in the Poyurovsky study were given only 40 to 80 mg of propranolol daily.

For patients with uremia or liver metastases, try haloperidol (Haldol) (0.5 to 1 mg t.i.d.), prochlorperazine (Compazine) (5 to 10 mg every 6 to 8 hours p.o. or 25 mg every 12 hours p.r.), or olanzapine (2.5 to 5 mg p.o. or sublingual b.i.d. to q.i.d.). For those with brain metastases, try dexamethasone (4 to 10 mg b.i.d. to q.i.d.); and for those with anxiety, lorazepam (Ativan) (0.5 to 1 mg every 4 to 6 hours p.o. or sublingual) or hydroxyzine (Vistaril) (25 to 100 mg t.i.d. or q.i.d.). Despite what your hospice colleagues tell you, the lorazepam (Ativan), diphenhydramine (Benadryl), and haloperidol (Haldol) in ABH gels do not reach therapeutic levels after being rubbed into the skin (Smith et al. 2012). If they decrease nausea, it is because of the decreased anxiety and the soothing nature of rubbing the gel into the skin. Do not substitute a gel for an oral, intravenous, or rectal formulation of any of these agents.

Treatment-Induced Nausea and Vomiting

Chemotherapy-induced nausea and vomiting plagues patients with cancer. Without adequate antiemetic therapy, 60 to 80 percent of patients receiving chemotherapy experience nausea and vomiting. Fortunately, over the past fifteen years, advances in the understanding of treatment-related nausea and vomiting have changed the lives of cancer patients, their families, and the nurses and doctors who care for them. When I began in oncology, we were sometimes unable to give even curative chemotherapy, such as treatment for testicular cancer, because

the available antiemetics were totally ineffective against the side effects induced by such drugs as cisplatin. Many of the cancer cures we now see are attributable to the revolution in the treatment of nausea and vomiting.

Although nausea and vomiting continue to plague a minority of patients, you can now prevent both the immediate and the delayed nausea and vomiting in 75 percent of patients receiving the drugs that cause the worst symptoms, and you will do much better with drugs that are less toxic (Basch et al. 2011; MASCC 2011). Your patients and their families are suffering less, and your burden, as a clinician, is much lighter.

Certain patients are at significantly higher risk of developing nausea and vomiting when they receive chemotherapy. Patients at highest risk are women and those younger than 50 years of age (Basch et al. 2011). Patients who are able to tolerate a large amount of alcohol will have less emesis induced by cisplatin therapy. Patients who have a history of alcohol intake of more than five alcoholic drinks per day (>100 g of alcohol) tend to have less nausea and vomiting than other patients receiving the same dose of drug and the same antiemetic protection (Blanchard and Hesketh 2011).

Pathophysiology. The most likely mechanism for acute and delayed chemotherapy-induced nausea and vomiting is stimulation of a neural network in the medulla oblongata called the central pattern generator. A number of neurotransmitters are thought to be involved, including serotonin, dopamine, and substance P. Drugs that block type 3 serotonin receptors (5-HT3 receptors), dopamine (D-2) receptors, and neurokinin (NK-1) receptors, if used along with dexamethasone, are able to prevent most chemotherapy-induced nausea and vomiting (Basch et al. 2011; MASCC 2011). How dexamethasone works remains a mystery, but when it is not included in the antiemetic regimen, patients experience significantly more delayed nausea and vomiting (Roscoe et al. 2012).

Vomiting that occurs within a day of receiving chemotherapy is considered "acute," and that occurring from the second to fifth day after treatment is considered "delayed."

Patients can also develop "anticipatory" nausea and vomiting as a classic conditioned response. Patients who develop nausea from chemotherapy learn to pair the office sights, smells, and sounds with the nausea and vomiting they experience there or shortly thereafter. Having motion sickness (Leventhal et al. 1988; Morrow 1984), being aware of tastes or odors during infusions, being generally anxious, and having acute or delayed chemotherapy-induced nausea or vomiting—all increase the odds of developing anticipatory nausea and vomiting (Andrykowski and Jacobsen 1993; Blanchard and Hesketh 2011).

RISK FACTORS FOR CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

- History of acute chemotherapy-related nausea or vomiting
- Emetogenicity of drug
- Age <50
- Female sex
- Low alcohol intake
- Generalized anxiety
- Awareness of tastes or odors during infusions

Unfortunately, patients with anticipatory nausea and vomiting do not need to be getting chemotherapy to become ill. Simply being in your office or seeing people whom they associate with it can cause them to vomit, even when they're nowhere near your offices. Imagine the scene as I greeted a former patient I encountered unexpectedly at an airport. I watched her smile turn to distress as the conditioned reflex took over! I felt nearly as bad as she did.

Therapy. The best way to prevent both anticipatory and delayed nausea and vomiting is to eliminate the acute symptoms by giving aggressive preventive antiemetic therapy before and after the chemotherapy infusion. Fewer than 15 percent of patients who do not experience acute nausea and vomiting will go on to develop delayed nausea or vomiting; 50 percent of those who do have acute problems will develop delayed vomiting, and 75 percent will have delayed nausea (Roila et al. 2002).

Both nonpharmacologic and pharmacologic approaches are effective for patients with anticipatory nausea and vomiting. Nonpharmacologic therapies include hypnosis (NCCN 2013; Redd et al. 1982), progressive muscle relaxation with guided imagery (NCCN 2013; Buish and Tope 1992), systemic desensitization (NCCN 2013; Morrow and Morrell 1982), distraction techniques (Redd et al. 1987), music therapy (NCCN 2013), and acupuncture or acupressure (NCCN 2013). Lorazepam (0.5 to 2 mg on the night before and the morning of treatment) or alprazolam (0.5 to 2 mg p.o. t.i.d. beginning on the night before treatment) are particularly useful agents for these patients (NCCN 2013). They cause amnesia for the events surrounding the chemotherapy and decrease anxiety (Laszlo et al. 1985).

At DFCI, clinicians created antiemetic therapy order sets using the ASCO consensus guidelines to prevent acute or delayed nausea and vomiting caused

by emetogenic chemotherapy (Basch et al. 2011; MASCC 2011). The guidelines recommend basing the choice of antiemetic agent(s) on the emetogenic potential of the chemotherapy or radiotherapy regimen (Tables 9.4 and 9.5), the side-effect profile of the antiemetic agent(s), and patient preferences and characteristics. For patients without prescription programs, the cost differences may dictate the outpatient regimen for the days following chemotherapy.

The side effects of the drugs often vary by age. Younger patients have a higher incidence of chemotherapy-induced nausea and vomiting. Therefore, even when they are receiving only moderately emetogenic therapy, they may need the multidrug regimen normally prescribed to prevent symptoms in patients receiving drugs of high emetogenicity (Johnson et al. 1997). Younger patients can tolerate cannabinoids (such as Marinol) better than older patients can and therefore find them more effective (Chang et al. 1979). But patients under 30 years of age receiving metoclopramide have a much higher risk of trismus or torticollis than patients over 30 (27 percent vs. 2 percent) (Kris et al. 1983). Elderly patients, on the other hand, have a high risk of extrapyramidal side effects from metoclopramide (Johnson et al. 1997).

5-HT3 Receptor Antagonists. The 5-HT3 receptor antagonists are extremely effective for patients with acute nausea and vomiting. The most effective of these agents appear to be ondansetron, granisetron, and palonosetron. They are given orally or intravenously, usually along with dexamethasone, to patients receiving moderate or highly emetogenic chemotherapy (Basch et al. 2011; MASCC 2011). When these agents are given along with dexamethasone, 75 percent of patients have no acute vomiting. Palonosetron blocks the 5-HT3 receptor for as long as 40 hours. Ondansetron (8 mg p.o. b.i.d) and granisetron (2 mg p.o. daily) are also recommended with or without dexamethasone (4 mg daily p.o.) for emesis induced by single- or multiple-fraction radiation therapy (NCCN 2013).

Ondansetron and the other 5-HT3 receptor antagonists have far fewer side effects than metoclopramide. Reports of extrapyramidal reactions are very rare (Halperin and Murphy 1992). The side effects often seen with metoclopramide (i.e., dystonic reactions, akathisia [severe restlessness, "ants-in-the-pants" feeling], sedation, and tardive dyskinesias) do not occur. Patients often develop constipation, and may develop mild headache and elevations in transaminases (Blanchard and Hesketh 2011). QTc prolongations occur at higher doses of ondansetron, and the recommendations therefore suggest that the maximum daily dose be 24 mg/day. Palonosetron has shown minimal prolongation of the QTc in limited studies.

Corticosteroids. We still do not understand how corticosteroids prevent nausea and vomiting. Some have suggested that they relieve the cerebral edema in-

duced by chemotherapeutic agents, such as cisplatin (Roila et al. 2002). Corticosteroids can be used either alone, when the chemotherapy has only low or moderate potential to cause vomiting, or as part of a regimen with a 5-HT3 antagonist or an NK-1 inhibitor (Basch et al. 2011; MASCC 2011). Dexamethasone and methylprednisolone are the best-studied agents, but no trials have demonstrated the superiority of one corticosteroid over another.

NK-1 Inhibitors. Substance P, a neurotransmitter that plays a key role in the transmission of the pain signal, can also cause vomiting, and it appears to play a role in chemotherapy-related nausea and vomiting. Its effects are mediated through NK-1 receptors. Agents that cross the blood-brain barrier and act as NK-1 inhibitors (e.g., aprepitant, fosaprepitant) are particularly effective in decreasing the delayed nausea and vomiting occurring after cisplatin chemotherapy (Basch et al. 2011; MASCC 2011).

Aprepitant itself has few side effects, but it is an inhibitor of CYP3A4 and therefore may elevate levels of dexamethasone and chemotherapeutic agents primarily metabolized by this route. Aprepitant can also cause significant decreases in the prolongation of the international normalized ratio (INR) induced by warfarin. Patients will have less nausea and vomiting if they take aprepitant as part of the antiemetic regimen both on the day of chemotherapy and for two days after their last dose of chemotherapy for each cycle (Basch et al. 2011; MASCC 2011). Patients take 120 mg on day one, followed by 80 mg on days two and three after a single-dose chemotherapy treatment, but they take 80 mg/day of aprepitant for seven days with a five-day regimen that includes cisplatin infusion (Albany et al. 2012). Fosaprepitant is given intravenously on day one and has not been found to be inferior to aprepitant in preventing the nausea and vomiting of patients treated with cisplatin (Grunberg et al. 2011).

Ginger. Pretreatment with ginger, which is known to bind 5-HT3 receptors, may be an effective adjuvant antiemetic. Patients who had experienced nausea with previous moderately emetogenic chemotherapy cycles were given dexamethasone and a 5-HT3 inhibitor, and then randomized to receive in addition either capsules containing a ginger suspension or placebo for three days prior to and three following chemotherapy. Patients receiving ginger had significantly less acute nausea on day one of chemotherapy, but the effect decreased in the post-chemotherapy period, days two to four (Ryan et al. 2012).

Other Agents. For patients who are not responding to these drugs alone, adding haloperidol, droperidol, prochlorperazine, scopolamine, or the atypical antipsychotic olanzapine may be helpful (NCCN 2013). Many of these agents, however, have significant side effects. Haloperidol and droperidol produce dystonic reactions, akathisia, QTc prolongation, and occasionally hypotension.

Transdermal scopolamine causes dry eyes and a xerostomia that can be intolerable. Olanzapine usually has few side effects, but it does lower the seizure threshold, prolong the QTc, and has been reported (rarely) to cause neuroleptic malignant syndrome or insulin-resistant diabetes.

Combination Antiemetic Therapy. For chemotherapeutic drugs with low or moderately low emetogenic potential, you may not need to give anything to prevent nausea, or you might give dexamethasone alone. For drugs of higher emetogenic potential, however, the guidelines recommend combinations of several antiemetic agents along with the agents mentioned above that are designed to treat anxiety, provide amnesia, or prevent known side effects.

The recommended combinations to prevent nausea and vomiting for moderately emetogenic chemotherapy include a 5-HT3 receptor antagonist such as ondansetron, a corticosteroid such as dexamethasone, and an optional anxiolytic such as lorazepam (Basch et al. 2011). To further lower the incidence of delayed nausea or vomiting, aprepitant or fosaprepitant (NK-1 inhibitors) should be included in the antiemetic combination for patients (1) with several risk factors that put them at high risk for developing delayed nausea and vomiting, (2) receiving highly emetogenic combination chemotherapy, or (3) receiving both adriamycin and cyclophosphamide (Basch et al. 2011; MASCC 2011).

PREVENTION OF ACUTE AND DELAYED NAUSEA AND VOMITING

Emetogenic Risk	*Day 1 Therapy*	*Day 2 to Day 4*
High or on AC	Dex + 5-HT_3 RA+ NK-1 inhibitor	Dex d 2–4 + NK-1 d2,3 or fosaprepitant d1 only
Moderate	Dex + 5-HT_3 RA	(Dex day 2–4)

(From Basch et al. 2011)

Note: Level of risk is based on emetogenicity of the drug. AC = Adriamycin + cyclophosphamide therapy.

Malignant Bowel Obstruction–Induced Nausea and Vomiting

The extent of the evaluation of a patient with a malignant bowel obstruction depends on the presumed etiology of the obstruction, the likely responsiveness of the cancer to specific antineoplastic therapy, the patient's nutritional status, and the patient's wishes for aggressive therapies. Soriano and Davis provide an

excellent review of the evaluation and therapeutic options for patients with advanced disease (Soriano and Davis 2011). Consultation with a surgeon (DeBernardo 2009) or gastroenterologist who specializes in treating patients with malignant bowel obstruction is often indicated. Palliative surgery or insertion of a self-expanding metal stent to relieve gastric outlet or proximal small bowel can be helpful for selected patients (Katsanos et al. 2010), often those who are not elderly and do not have ascites, peritoneal carcinomatosis, previous radiation to the pelvis, or evidence of multiple sites of obstruction (Ripamonti et al. 2008). Whether or not stenting of the colon is a helpful bridge to surgery remains controversial, but the evidence seems to suggest that stents are not helpful in this role (Tan et al. 2012; Sagar 2011; NIHCE 2011).

PRACTICE POINTS: TREATING BOWEL OBSTRUCTION IN PATIENTS WHO ARE NOT CANDIDATES FOR SURGERY

- Gastric outlet obstruction:
  - —NG tube; evaluate for a self-expanding metal stent or venting gastrostomy (PEG)
  - —Medical therapy: dexamethasone + octreotide + analgesics (± metoclopramide)
- Lower intestinal obstruction:
  - —Initial: Dexamethasone + opioids; consider glycopyrrolate or scopolamine patch, for persistent nausea, vomiting, and cramping abdominal pain.
  - —If only a partial bowel obstruction or an ileus, add metoclopramide (10 mg IV q6h or 1 to 2 mg/hr) rather than glycopyrrolate or scopolamine
  - —Persistent obstruction: NG tube if not already in place; Discontinue scopolamine or glycopyrrolate (if complete obstruction, discontinue metoclopramide) and add octreotide 300 to 600 μg / 24 hr SQ in divided doses (b.i.d. or t.i.d.).
  - —For responders to octreotide: administer depot version (e.g., LAR octreotide) monthly, 20–30 mg deep IM; continue SQ octreotide for ≈14 days after depot is given.

Before surgery, stenting, or medical therapy provide more definitive relief, nasogastric (NG) intubation is often required as a temporary measure. Patients with only a partial bowel obstruction or an ileus often respond to the motility agent metoclopramide (5 to 10 mg IV every 6 hours or 1 to 2 mg/hr). Its procholinergic activity enhances gastric motility, and, to a lesser extent, motility in the

jejunum, ileum, and colon. If cramping increases, however, the obstruction may be worsening; the metoclopramide should be discontinued and anticholinergic agents added.

Medical treatment for patients with more advanced bowel obstructions includes decompression with an NG tube, opioids, and dexamethasone; anticholinergic agents (e.g., glycopyrrolate, hyoscyamine, and scopolamine) can also be considered for patients who have a great deal of cramping abdominal pain. The anticholinergic activity decreases motility and therefore abdominal colic, so that opioids can be minimized. Anticholinergics also activate muscarinic receptors, and so decrease the secretion of water, sodium, and chloride. Scopolamine, however, often produces excessively dry mouth and eyes as well as mydriasis, and because it crosses the blood-brain barrier, it can increase the chance of the patient becoming delirious.

For patients who cannot tolerate anticholinergic agents, or whose obstruction does not respond to the combination of these agents, stop the anticholinergic agents and add octreotide. If the obstruction is not complete, octreotide is often very effective. It is a synthetic analogue of somatostatin, and as such, it inhibits secretion of growth hormone, gastrin, secretin, vasoactive intestinal peptide, pancreatic polypeptide, insulin, and glucagon, as well as blocking the secretion of gastric acid, pepsin, pancreatic enzymes, bicarbonate, and, probably most important for these patients, intestinal epithelial water and electrolytes.

A typical patient who would benefit from octreotide is someone with advanced ovarian cancer whose symptoms are due to recurrent bowel obstruction by tumor implants or adhesions. At doses of 150 to 300 μg subcutaneously, twice daily (or 300 to 600 μg/24 hr continuous SQ infusion), octreotide has produced major improvements in these patients' lives. In about three days (range, one to six days), it can eliminate the nausea and vomiting in the majority of patients for whom it is tried and dramatically decrease the volume of nasogastric drainage (Mercadante and Porzio 2012).

Patients who respond to SQ octreotide and are expected to have persistent bowel obstruction should be given an intramuscular injection of the LAR form of octreotide monthly. The octreotide is released from a microsphere polymer matrix, and it takes two to three weeks for therapeutic blood levels to be achieved. Patients need to continue taking their SQ octreotide, therefore, for two to three weeks after the LAR injection (Prommer 2008). A new somatostatin analogue, lanreotide formulated in microparticles, was somewhat more effective than placebo in reducing vomiting after NG tube removal as well as improving well-being (Mariani et al. 2012).

In 2006, Laval and colleagues published the results of their prospective study of patients who required medical therapy for a malignant bowel obstruction (Laval et al. 2006). As of 2013, no randomized controlled trials have appeared, and this study is the largest prospective study reported to date. This study followed 75 consecutive patients with peritoneal carcinomatosis (80 obstructive episodes). The largest group had cancer of the ovary (21 patients) or colorectal cancer (19 patients); 10 had pancreatic and 9 had esophageal or stomach cancer. For the first five days, patients had a NG tube placed and received a corticosteroid (Solumedrol 1-4 mg/kg), an antiemetic (haloperidol 1-5 mg / 8 hr or chlorpromazine 25–50 mg / 8 hr or continuous IV or SQ pump), an anticholinergic agent (scopolamine), and analgesics as needed. If they got relief, the corticosteroids and antisecretory drugs were tapered off. If they were still obstructed or the NG tube was putting out more than 1L / 24 hours, in addition to the drug taper, they received octreotide 200 μg every 8 hours or 600 μg/day by continuous infusion. If the patient was still refractory to therapy three days later, a venting gastrostomy tube or, when possible, a stent was placed.

This protocol was very effective. The median time to controlled symptoms was five days. Fifty of 80 obstructive episodes improved in the first five days. In 25 of those 50, the obstruction was relieved. It was most effective in corticosteroid-naive patients: 20 of 25 whose obstruction was relieved had not received previous corticosteroids. The obstruction resolved in only 30 of 55 who had received previous steroids ($p < .03$). Of the remaining 30 patients, the addition of octreotide relieved the obstruction in 4 patients, and an additional 7 achieved symptom control.

Nausea and Vomiting of Unclear Etiology

Symptomatic therapy is used for patients with nausea of unclear etiology. A systematic review of the studies on nausea or vomiting not caused by radiation or chemotherapy concluded that the studies were inadequate to provide definitive recommendations (Davis and Hallerberg 2010).

Most of the available guidelines are based on expert opinion. What follows, therefore, is my "expert opinion." Metoclopramide (Reglan) (5 to 10 mg p.o. / SQ or IV every 6 hours or 1 hour before meals) is a useful first-line empirical nausea treatment. At this dose, it is associated with few side effects. If nausea persists, add dexamethasone (4 mg p.o. or SQ b.i.d.). If the patient remains nauseated 48 hours after the dexamethasone is added, discontinue the metoclopramide and dexamethasone and add olanzapine.

Olanzapine is an atypical antipsychotic agent that blocks the receptors of several neurotransmitters, including dopamine and serotonin. Weight gain is a serious problem for patients without cancer who take olanzapine. It is not surprising, then, that a series of case reports indicate that it is effective against nausea of unclear etiologies in patients with cancer. It rarely causes extrapyramidal side effects. Doses start at 2.5 mg at bedtime and can be increased to 5 mg four times as needed. If olanzapine is not effective, discontinue the olanzapine and try ondansetron (Zofran) (4 to 8 mg p.o. b.i.d. to t.i.d.), lorazepam (0.5 to 1 mg p.o. b.i.d. to t.i.d), or haloperidol (Haldol) (1 to 2 mg p.o. b.i.d. to q.i.d.). For patients who do not mind the associated alterations in mental status, dronabinol (tetrahydrocannabinol) (Marinol) (2.5 to 10 mg p.o. b.i.d. to t.i.d., or higher as needed and tolerated) can be an effective oral antiemetic. Unfortunately, its oral absorption is somewhat variable. Data on the vaporized tetrahydrocannabinol:cannabidiol (THC:CBD), used for pain control, are not available for nausea, though it is likely to be well absorbed, and therefore effective, and have the same side-effect profile as dronabinol. The integrative therapies for nausea, such as hypnosis, acupuncture, and mindfulness-based stress reduction, are discussed in Chapter 7.

Respiratory Problems

Dyspnea

Dyspnea is frightening to patients with advanced cancer and to their families, who fear they will die a death of suffocation. It creates significant problems in about 40 percent of these patients. In the National Hospice Study (Reuben and Mor 1986), dyspnea was found to occur in as many as 70 percent of cancer patients at some time during their last six weeks of life. You may not realize that a patient is experiencing dyspnea if you rely solely on observing tachypnea. In one study of hospice patients, 77 percent of patients reported dyspnea, but only 39 percent were recorded as having dyspnea (Thomas and von Gunten 2003).

Pathophysiology. Dyspnea is mediated by (1) J-receptors at the junction of capillaries and alveoli, which respond to alveolar fluid or to microemboli; (2) mechanoreceptors in the lungs, airways, and chest wall that respond to stretch; (3) peripheral chemoreceptors in the aorta and carotid bodies that respond to hypoxemia; and (4) central chemoreceptors that respond to increases in carbon dioxide. When the CO_2 rises to 75 mm Hg, endorphins are released centrally, causing the dyspnea to abate and the patient to become somnolent.

Patients experience dyspnea in one of three situations: when breathing requires more work (e.g., with interstitial lung disease or pleural effusions); when the

patient is hypercapnic; and when the brain perceives less ventilation than it "expects" from the amount of work being done to provide the ventilation. The brain receives input on the work the muscles are doing, and "expects" a certain amount of return on the investment in terms of flow rate of air. When there is less airflow than expected, the patient experiences dyspnea. Patients who are not hypoxemic, therefore, can still be dyspneic. But oxygen therapy is no better than nasal air for them (Clemens et al. 2009). The nasal air infusion "tricks" the mechanoreceptors into thinking the muscles are doing more work than they are.

Etiology. In 25 percent of patients with dyspnea, no specific cause will be identified, but muscle weakness or anxiety may contribute. In the other 75 percent, a thorough physical exam and a few simple tests (e.g., chest x-ray, electrolytes, complete blood count, and pulse oximetry) are likely to reveal the cause of the dyspnea. The most common etiologies are pulmonary or cardiac pathology, ascites, anemia, and superior vena cava syndrome.

Pericardial effusions and tamponade are particularly subtle causes of dyspnea in cancer patients. Tumor infiltrating the pericardium causes it to become thick and rigid, and even a small amount of fluid can significantly impair cardiac filling. Because of the rigidity of the invaded pericardium, chest films may show a normal heart size even when tamponade is present. Have a high index of suspicion when a patient with known mediastinal disease—or, more commonly, with a left-side pleural effusion even after the fluid is drained—remains anxious and dyspneic.

Superior vena cava syndrome is most often seen in patients with lung cancer, though lymphoma and other cancers each cause about 10 percent of cases, with a smaller contribution from clotted indwelling central venous catheters. In addition to dyspnea, patients may have headache or blurred vision and appear plethoric, with facial, neck, and upper extremity edema in advanced cases. Chest films reveal disease in the right upper mediastinum, and radionuclide or MRI studies show compression of the superior vena cava with decreased flow.

Therapy. Anxious patients are likely to benefit from both pharmacologic and nonpharmacologic therapies (Ben-Aharon et al. 2008). Lorazepam (0.5 to 2 mg every 4 to 6 hours p.o. or sublingual), clonazepam (0.5 to 1 mg p.o. at bedtime or b.i.d.), or the other agents listed in Table 9.1 are helpful to decrease anxiety in the average patient. For very anxious patients or patients in an uncontrolled panic due to a perceived inability to breathe, give midazolam (0.2 to 0.5 mg IV very slowly); morphine (2 to 5 mg IV or by nebulizer), or another opioid at an equivalent dose; or chlorpromazine (12.5 to 25 mg p.o. or IV). Morphine and midazolam (Ben-Aharon et al. 2008) or lorazepam (Clemens and Klaschik 2011) have been given together without inducing respiratory depression.

Relaxation techniques or formal hypnotic imagery may be effective adjuncts that skilled practitioners, including members of the hospice team, can teach to patients and their families. Medical practitioners of hypnosis are listed in the directory of members of the American Society of Clinical Hypnosis (www.asch.net).

When possible, and as appropriate, reverse the specific medical cause of the dyspnea. Because dyspnea can be so distressing, it is reasonable to consider somewhat aggressive attempts to reverse obstruction of bronchi, blood vessels, or lymphatics to decrease the dyspnea. External beam or endobronchial radiation therapy, laser treatments, cryotherapy, and stents all can reopen blocked airways. For some patients whose bronchial obstruction is not relieved, radiation therapy still relieves the dyspnea, possibly by decreasing compression of the surrounding blood vessels and lymphatics.

About 70 percent of patients with superior vena cava syndrome will respond to radiation therapy for a median of about 3 months. High-dose corticosteroids are also usually included; they are tapered after a week if no benefit is observed or after the end of radiation treatments. High-dose corticosteroids alone (e.g., 80 mg solumedrol IV t.i.d for 3 days) can ameliorate dyspnea in patients with lymphangitic tumor spread, possibly by inhibiting the inflammatory reaction to the tumor and lessening alveolar capillary fluid leak.

Blood transfusion may be tried for hypoxia due to anemia, and pericardiocentesis or pericardial window for pericardial effusion. Oxygen is helpful only in hypoxemic patients (Ben-Aharon et al. 2008) and is indicated even for patients who retain CO_2 to maintain an oxygen saturation of 88 to 90 percent (pO_2 of 55 to 60 mm Hg). Nebulized furosemide may possibly be helpful in alleviating dyspnea (Ben-Aharon et al. 2008).

Pleural effusions are a frequent cause of dyspnea in patients with lung or breast cancer, but also occur in patients with other kinds of cancer. For patients who are not physically active, symptoms can often be controlled with supplemental oxygen (for those who are hypoxemic) and/or opioids. Although one would think that benzodiazepines decrease the anxiety associated with dyspnea, a recent Cochrane review questioned the efficacy of their use (Simon et al. 2010).

Symptomatic therapy is especially appropriate for very debilitated patients whose prognosis is so short that they are not candidates for surgical drainage of their effusions. In one study, patients with malignant pleural effusions who had leukocytosis, hypoxemia, and hypoalbuminemia had a median survival of only 42 days, compared with those with none of those factors who lived a median of 702 days ($p < .00001$) (Pilling et al. 2010).

Other patients will achieve relief only when the effusions are drained. Because the effusion reaccumulates within one month in 97 percent of treated

patients, most patients with malignant effusions will need more than a simple thoracentesis. Sclerotherapy has been done with bleomycin (Moffett and Ruckdeschel 1992) and doxycycline, but talc slurries inserted via thoracoscopy have been shown to be most effective (Shaw and Agrawal 2004; Dresler et al. 2005). The chemotherapeutic drug mitoxantrone (40 mg) is another effective sclerosing agent. Infused after chest tube drainage, mitoxantrone induced a complete remission in all 20 patients in which it was used, and none experienced fluid reaccumulation in the ensuing two months (Morales and del Carmen Exposito 1995).

Some patients have such extensive effusions or such a high rate of fluid production that the pleural space cannot be drained dry enough for a sclerosing agent to be effective; in others, despite adequate drainage, the lung will not re-expand. The quality of life of such patients may be severely impaired by the effusions or the collapsed lung. For those with a reasonable life expectancy (e.g., patients with breast cancer or lymphoma), a surgical procedure may be helpful.

Some surgeons believe that for patients who can tolerate general anesthesia, an open procedure is indicated; they can decide at surgery whether to use talc pleurodesis or to insert a pleural catheter. If, after the fluid is drained, the lung re-expands fully, the surgeon uses talc as an irritant. This has been successful in preventing recurrent effusions in more than 90 percent of those undergoing such a procedure. If, however, the lung does not re-expand, the surgeon inserts a pleural catheter (e.g., PleurX).

In one randomized trial, the Denver PleurX pleural catheter was as effective as a chest tube and sclerosis in improving dyspnea and quality of life in patients with malignant effusions (Putnam et al. 1999). The PleurX catheter is a 15.5 French silicone catheter with a fenestrated length of 24 cm and a polyester cuff to reduce infection risk. The catheter's fenestrated end is situated in the pleural space, and several inches of its mid-portion, including the cuff, are tunneled subcutaneously, leaving the end of the catheter and valve exposed so that the patient can drain the fluid. Patients use a special drainage kit as often as their effusion requires.

In the trial, patients with these catheters went home much earlier (median length of hospitalization, 1 day vs 6.5 days; $p < .0001$). The patient drained the pleural fluid at home; spontaneous pleurodesis occurred in 46 percent (median time, 29 days). Complications of insertion occurred in 10 percent (10 of 96 patients). Three patients each had fever or pneumothorax, two had misplacement of the catheter, one had reexpansion pulmonary edema, and one had hypercapnic respiratory failure from oversedation. Late recurrences (21 percent), pain severity, and early inpatient complications (10 to 14 percent) were similar in both groups. Several subsequent reports have also confirmed the safety and utility of these catheters (Pollak 2002).

For the 25 percent of patients for whom no specific cause of dyspnea can be identified, symptomatic treatment is still possible. For these patients and for those in whom we cannot reverse the underlying cause, a variety of therapies will significantly relieve their distress (Table 9.6).

Something as simple as sitting in front of an open window or having a fan blowing air softly onto the face provides significant relief for some. The most useful treatment, even for cancer patients taking high doses of systemic opioids, is an oral, subcutaneous, or intravenous opioid. Nebulized morphine did not improve the dyspnea score (as measured by VAS) better than the subcutaneous route, but patients may prefer the nebulized route (Ben-Aharon et al. 2008). The opioid is often combined with dexamethasone. Typical starting doses are 2.5 to 5 mg of morphine given orally; or for nebulized therapy, 2.5 to 5 mg of preservative-free morphine or 1 mg of hydromorphone (Dilaudid) and 2 mg of dexamethasone in 2.5 ml of 0.9 percent saline every 4 hours as needed. If wheezing is present, albuterol (0.5 ml) can be added as well. The mixture is given by a nebulizer using room air or oxygen at 5 to 6 liters/minute through an open facemask.

The opioid dose should be increased as needed until the dyspnea is relieved. Reports from the Leicestershire Hospice indicate that doses of up to 50 mg have been used. In some individuals, inhaled morphine causes bronchospasm (Ahmedzai 1997). Administration of the first dose should therefore be observed by a nurse or other clinician who can provide antiasthma treatment if needed.

For patients who develop bronchospasm, substitute fentanyl, which does not induce bronchial histamine release. Nebulized fentanyl (25 μg in 2 ml of saline) was shown to improve oxygenation and decrease respiratory rate in a convenience sample of 35 cancer patients (i.e., all patients who agreed to participate in the trial) (Coyne et al. 2002). Ninety-one percent reported improvement in breathing within five minutes of the treatment, and that improvement lasted at least an hour. Small doses of nebulized opioids are thought to be effective because the opioids act directly on opiate receptors in the large airways. However, the Cochrane review found no benefit for nebulized opioids over other routes of delivery (Jennings et al. 2001).

Cough

Etiology. Cough, present in about 40 percent of patients with advanced cancer, is caused by many of the same disorders that cause dyspnea. It is mediated by stimulation of the vagus nerve by receptors in the pharynx, larynx, and upper airways and by airway opiate receptors.

Cough can occur in patients with postnasal drip, infection, heart failure, asthma, chronic obstructive lung disease, esophageal reflux, or those taking ACE inhibitors. Specific cancer-related causes include both obstruction of the airway and disorders of swallowing. Swallowing disorders can be due to ischemic vascular disease or brain metastases, injuries of the ninth and tenth cranial nerves from local or metastatic tumor invasion or carcinomatous meningitis, impairment of the recurrent laryngeal nerve by tumor in the left hilar area, or tumor of the head and neck or esophagus. Such patients can aspirate their routine secretions, and cough can be their most troubling symptom.

Therapy. Specific therapies are used for the causes listed above. Laser or radiation therapy may resolve a distressing cough due to an airway obstruction. For those without an obstruction whose cough is productive, chest physical therapy, humidity, and suctioning can help.

Various pharmacologic agents for symptomatic treatment of cough are listed in Table 9.6. Benzonatate (Tessalon Perles) (one or two p.o. t.i.d.) has an anesthetic action that numbs the stretch sensors in the lower airways and lung and so prevents the coughs induced by deep breathing. Relief starts within 15 minutes and the effect of each dose can last for several hours. Hyoscyamine (Levsin) or scopolamine (Transderm Scōp) can decrease excessive secretions. For patients who cough because of tenacious mucus, nebulized saline, albuterol (0.5 mg in 2.5 mg of normal saline), or terbutaline have been helpful, while expectorants such as guanefesin and mucolytics have not. Since ipratropium worsens this problem, discontinue it when possible.

When specific therapy is unavailable or ineffective, oral opioids are the most effective nonspecific therapies for cough. Initially, try sweet elixirs containing dextromethorphan or one of the opioids used for mild pain; methadone syrup, if available, can also be useful.

For more resistant coughs, higher doses of oral or nebulized opioids (see Dyspnea, above) may be needed. In addition, nebulized anesthetics (e.g., 2 ml of 2 percent lidocaine in 1 ml of normal saline for 10 minutes) can be given up to three times a day. Unfortunately, the anesthetics cause patients to lose their gag reflex temporarily. To avoid aspiration, ask patients to fast for about one hour after a nebulized anesthetic treatment. Since some patients develop bronchospasm after nebulized anesthetics, the first dose should be taken under close observation.

Hemoptysis

Although 50 to 70 percent of patients with lung cancer complain of hemoptysis, it is a problem for only about 25 percent of those admitted to hospice.

Despite its relative rarity, however, hemoptysis is one of the most frightening symptoms that patients experience. Letting the family know what to do should the hemoptysis worsen and advising them to use red or dark-colored bedding and towels, on which the blood is less apparent, may lessen their anxiety. (For a discussion of the management of patients with massive hemoptysis, see Chapter 10.)

As in patients without cancer, hemoptysis in cancer patients may be due to bronchitis, pneumonia, or a pulmonary embolism. In patients with cancer of the head and neck or lung, however, it is often due to cancer recurrence. Even for patients who have previously received radiation treatment, small amounts of additional radiation can control the bleeding in almost 90 percent. Bronchial lavage with iced saline, topical epinephrine, topical fibrinogen-thrombin solutions, balloon tamponade, and laser therapy may also be helpful. Embolization of the portions of the bronchial artery involved has been found to be particularly effective for patients with bronchiectasis and inflammation, but more than half of the cancer patients embolized also stopped bleeding (Hayakawa et al. 1992). The optimal therapy for a given patient, therefore, may depend both on the site of bleeding and on the radiation, pulmonary, and angiographic expertise that is available.

Hiccups

Hiccups are embarrassing and exhausting, and they interfere with a patient's ability to eat, drink, and sleep.

Etiology. Although hiccups can occur in patients with any of one hundred different diseases, the most common causes are gastroesophageal reflux disease (GERD) or gastric distension, problems in the chest or lung, or problems in the central nervous system (Calsina-Berna et al. 2012). Eighty percent of the time, hiccups are caused by a unilateral contraction of the left hemidiaphragm, and the problem is almost always (91 to 99 percent of the time) self-limited (Calsina-Berna et al. 2012).

Hiccups may occur in patients whose vagus or phrenic nerves are injured (anywhere in their course) or who have certain metabolic derangements (especially uremia, but also hyponatremia or hypocalcemia). Patients can develop hiccups as a side effect of benzodiazepines, barbiturates, progesterone, anabolic steroids, intravenous corticosteroids, or, more rarely, chemotherapy (e.g., cisplatin) or hydrocodone. Occasionally, you will find a previously unidentified ear infection, pharyngitis, or esophagitis, which, if treated effectively, may end the hiccups, as may treating ascites, pneumonia, pleuritis, or pericarditis. The sys-

tematic review by Calsina-Berna and colleagues offers an exhaustive list of potential causes (Calsina-Berna et al. 2012).

Therapy. The nonpharmacologic treatments are those we've all used: granulated sugar, drinking from the far side of a glass, rubbing the back of the neck with a cool cloth, holding one's breath, or doing a Valsalva maneuver while breath-holding. Acupuncture was effective in one retrospective series. For selected patients with intractable hiccups, phrenic nerve block (e.g., with bupivacaine) or lysis may be required, but these treatments are rarely needed.

Some pharmacologic treatments are listed in Table 9.6. Baclofen, gabapentin, and chorpromazine are the best studied. Baclofen is started at 5 to 10 mg p.o. t.i.d and may be increased as needed, and concomitant alcohol use should be avoided to prevent excessive sedation. Gabapentin, which blocks calcium channels, improved hiccups in 83 percent of patients in one retrospective chart review, at a dose of 300 mg initially, increasing to 1200 mg if needed; pregabalin is likely to be equally effective. Chlorpromazine (Thorazine) (25 to 50 mg IV, then p.o. or p.r. t.i.d.) is very effective but it causes significant postural hypotension (Howard et al. 2011). Haloperidol (Haldol) (2 to 5 mg p.o. or p.r. or 0.5 to 2 mg IV) is probably equally effective but safer in older patients. Metoclopramide (5 to 10 mg p.o. q.i.d) is effective for patients with gastric distension; amantadine worked in a patient with Parkinson's disease (Wilcox et al. 2009), perhaps by improving the disease-associated gastroparesis. Hiccups due to GERD respond to proton pump inhibitors. Midazolam, nifedipine (10 to 20 mg p.o. t.i.d.), sertraline (50 to 100 mg/day p.o.), benztropine (Cunningham 2002), nefopam (Bilotta and Rosa 2000), and valproic acid have all been reported to be effective.

Skin Problems

Patients with cancer can have skin problems caused by the cancer or its treatment. A comprehensive treatment guide for these conditions is beyond the scope of this volume. Dr. Mario Lacouture, however, has written an excellent book for patients and their families (Lacouture 2012). In this section, I will review hand-foot syndrome, epithelial growth factor receptor (EGFR) inhibitor-associated toxicities, fungating skin lesions, pressure ulcers, and pruritis.

Hand-Foot Syndrome

Hand-foot syndrome (plantar-palmar erythrodyesthesia) was first described thirty years ago. It is a dose-limiting toxicity of infusional fluorouracil, capecitabine, and liposomal doxorubicin (Wolf et al. 2010). Patients experience toxicities that

range from erythema without pain to peeling, blisters, bleeding, edema, or pain, to a limitation of function due to worsening of those symptoms or pain. The mechanism of hand-foot syndrome is unknown, and the only effective treatment is to decrease the infusion of the offending agent. A urea and lactic acid–based keratolytic agent was not found to be effective in patients receiving capecitabine and may have actually worsened the symptoms in the first week of use (Wolf et al. 2010).

A different type of hand-foot skin reaction occurs in 14 to 62 percent of patients taking one of the tyrosine kinase inhibitors, sorafenib, sunitinib, lapatinib, or regorafenib (Manchen et al. 2011). The mechanism of this reaction is thought to be a simultaneous blockage of vascular endothelial growth factor receptors (VEGFRs) and platelet-derived growth factor receptors (PDGFRs) by these agents. In addition to the changes in the hands and feet, these patients develop facial erythema, scalp dysesthesia, alopecia, and subungual splinter hemorrhages (Manchen et al. 2011). As with hand-foot syndrome, the only effective treatment is decreasing the offending drug. Symptomatic therapies include using the "3C approach": "control calluses, comfort with cushions, and cover with creams" (Manchen et al. 2011, p. 22).

EGFR-Inhibitor–Associated Toxicities

EGFR-inhibitors are used to treat patients with a wide variety of malignancies, including lung, breast, head and neck, and colon and rectal cancers. They commonly cause a rash that resembles acne (80 percent); increased brittleness of the hair, alopecia, or hypertrichosis of scalp hair, eyelashes, and eyebrows; xerosis so severe that the skin develops fissures; paronychia; pruritus; and mucositis (Lacouture et al. 2011). Patients on EGFR-inhibitors also have worse radiation dermatitis than patients not taking them. If the toxicities are severe enough, doses of the offending agent or the radiation are reduced. Education and psychological support as patients' appearance changes are key elements of any treatment regimen.

The rash typically presents in the first two to four weeks of treatment. Aggressive prophylactic treatment with hydrocortisone (1 percent) combined with moisturizer, sunscreen, and doxycycline 100 mg twice daily for six weeks has been shown to diminish its severity (Lacouture et al. 2011). Minocycline 100 mg daily for eight weeks is also effective and less photosensitizing, but doxycycline has a better safety profile. If the rash worsens, high-potency topical corticosteroids and low-dose isotretinoin are recommended, though the evidence is not as good for these agents.

Minoxidil may help patients with nonscarring alopecia (Lacouture et al. 2011). Scarring alopecia may be lessened by topical hydrocortisone (0.2 percent), steroid shampoos, class 1 steroid lotions, bath oils, or mild shampoo followed by an antibiotic spray (Lacouture et al. 2011). Excess facial hair can be treated by eflornithine cream or hair removal; to prevent corneal abrasions, treat trichomegaly by clipping the eyelashes (Lacouture et al. 2011).

Lacouture and colleagues review symptomatic treatment for oral complications, xerosis and fissures, and paronychia in their discussion of clinical guidelines for the care of patients receiving these agents (Lacouture et al. 2011).

Fungating Skin Lesions

Fungating lesions from cancers growing out through the skin can cause embarrassment, shame, and profound loss of self-esteem, especially for patients who were previously proud of their appearance. Not only are the lesions painful, but the associated discharge and odor can be so offensive that even family members find it hard to remain near the patient.

Primary skin cancers, breast cancers, and cancers of the head and neck that become refractory to chemotherapy and radiation can cause fungating skin lesions, as can metastases. Patients with breast cancer are particularly prone to developing skin metastases on the chest wall or scalp, but they also occur in about 10 percent of those with renal cancer and 5 percent of those with other cancers. Chemotherapy and radiation can be effective, especially in reducing bleeding. Surgery should also be considered as a palliative measure, especially in recurrent breast cancer and extensive melanoma metastases.

Symptomatic treatment. Although these wounds rarely heal completely, symptomatic treatment is often effective for tumors that are refractory to specific modalities. Skin care protocols and tables of wound care products are included in the *Oxford Textbook of Palliative Medicine, Principles and Practice of Supportive Care in Oncology,* and *Handbook of Palliative Care in Cancer* (see General References in this chapter's bibliography). Hospitals and visiting nurse associations have policies and guidelines as well. Specially trained advanced-practice nurses are also valuable resources in caring for patients with decubitus ulcers, tumor metastases, skin infections, and other chronic skin wounds. Sarah Kagan, MSN, CRNP, a colleague of mine who is a geriatric nurse practitioner and wound care expert, and Ilene Fleisher and Diane Bryant, certified enterostomal therapy nurses, have generously contributed material for the recommendations that follow. For additional questions, use your visiting nurse association as a resource.

PRACTICE POINTS: CARE OF FUNGATING SKIN LESIONS AND PRESSURE ULCERS

- Keep the wound clean.
- Control odor.
- Gently debride it.
- Relieve pain (e.g., consider topical intrasite gel with 1% morphine for open skin areas).
- Use antibiotics and antifungals.
- Apply the correct, layered dressing.
- Control bleeding.
- For pressure ulcers: minimize shear forces and the time spent in one position; provide the correct mattress.

Wound Cleaning. Keep the wound clean by irrigating it with sterile saline, lactated Ringer's, or homemade saline solution (1 tsp. of salt dissolved in 1 pint of boiled water), or by showering. For wounds that are colonized with anaerobic organisms, consider applying metronidazole intravenous solution by gentle irrigation (e.g., pouring or through an irrigation syringe) or by applying gauze sponges soaked in metronidazole gel.

Debridement. Debride the wound gently, using continuous moist saline dressings. For dry but purulent tissue, use an enzymatic debriding ointment (e.g., collagenase, Accuzyme) or a gel such as Debrisan. Debrisan is composed of polysaccharide dextranomer granules, which can be poured in a clean, moist wound and covered with a semi-occlusive dressing. The granules will draw the bacteria and dead cells up out of the wound.

For wet, heavily exudative wounds, with or without colonization or obvious infectious findings, use absorptive dressings, which include hydrofibers, collagen, and calcium alginates; hydrophilic foams; and polymers such as cadexomers. These are widely available under many trade names, including Aquacel, Hydrofiber wound dressing, Kaltostat, Sorbsan, Iodosorb, and Allevyn. Avoid hypertonic saline dressings, which would literally put salt in the wound. To prevent the exudate from macerating the tissue, providing a medium for infection and embarrassing the patient, use absorbent foam topped by a thick gauze pad and an alginate dressing. The alginate dressings do not have to be removed; they wash off during bathing (von Gunten 2002).

Antibiotics. Consider adding topical or systemic antibiotics. Aerobic bacteria can easily superinfect fungating tumors. *Staphylococcus aureus* and other com-

mon pathogens often respond to topical antibiotics such as triple antibiotic ointment or mupirocin. Gram-negative organisms may be more prominent in anogenital areas, and you may need to recommend silver sulphadiazine cream and potassium permanganate sitz baths to prevent recurrent infection. Anaerobes respond to topical metronidazole; fungus to Nizoral or other ketoconazole creams; and painful viral lesions to acyclovir ointment.

Control of Bleeding. Widespread oozing can be controlled with a sucralfate paste, made by mashing a 1-gram tablet in a small amount of water-soluble gel. Gauze soaked in 1:1000 epinephrine solution, Gelfoam soaked in thrombin, Avitene, topical thromboplastin (100 μg/ml), or Surgicell can also be used. Silver nitrate sticks should be reserved for isolated bleeding points. Nonadherent, moist dressings can often decrease oozing by diminishing the trauma associated with dressing changes.

Control of Odor. Eliminate the bacteria that are causing the odor, which are mostly anaerobic. Despite its toxicity to the skin and newly budding capillaries, you may consider using a disinfectant solution such as quarter-strength Dakin's or 1 percent chlorhexidine gluconate as a first measure. Unfortunately, although these solutions are not expensive, they can cause discomfort and are not always effective. Most cases also require more expensive therapies: metronidazole gel (0.75 percent) applied to the lesion, along with oral metronidazole (200 to 400 mg p.o. t.i.d.) if needed. Metronidazole has been shown to be totally effective in 50 percent and reasonably effective in an additional 45 percent of patients for whom it was used.

Topical aromatherapeutics can be mixed into a bland base (e.g., vitamin A and D ointment) to provide odor control and a sense of well-being. Essential oils for first-line, nontoxic use are lavender (soothing, deodorizing); tea tree oil (antimicrobial, cleansing); and peppermint (deodorizing, cleansing). These should be added to the base at 10 to 30 drops per ounce.

If cost is an issue or metronidazole gel is not available, try applying Maalox, which may also relieve burning. Oral chlorophyll tablets can decrease the odor. Natural remedies such as applying yogurt or buttermilk, which prevent growth of odor-forming bacteria, or powdered sugar or honey, which compete with the bacteria for water, have also been effective in controlling odor. The yogurt can also relieve burning. One-quarter percent menthol may also be added to a bland base for topical antipruritic use on intact skin.

Pain Relief. A series of case reports suggests that topical opioids may relieve the pain of skin ulcers (Twillman et al. 1999). Morphine-infused IntraSite gel (0.1 w/w solution or 1 mg morphine / 1 ml IntraSite gel) is spread on a clean ulcer, then covered by a 4 × 4 inch gauze dressing; or the gel is placed on the

dressing, which is then applied to the wound to cover the entire ulcerated wound surface. New gel is applied when dressings are changed (usually twice a day). In a pilot randomized double-blind placebo-controlled crossover study, of five patients with decubitus ulcers, topical morphine provided significantly more pain relief than placebo (Zeppetella and Ribeiro 2003). No side effects were noted.

Wound Dressing. Wound dressings serve a number of purposes. They allow the removal of excess exudate, bacterial toxins, and dead skin cells; maintain a moist, clean environment; are relatively impermeable to bacteria; and provide comfort and protection from further injury. Unless the patient is neutropenic or there is a reason to use sterile technique, clean technique can be used, including clean gloves, for dressing changes at home.

For a dressing to accomplish all this, it must be made up of layers with different functions. The material closest to the skin should be sterile, should allow exudates to pass through it, and should not stick to the skin. Hydrocolloid dressings (Duoderm, Granuflex, hydrogel, Xero-form) are particularly useful if there is little exudate, because they are nonadherent and provide pain relief; alginate dressings (Kaltocarb, Kaltostat, Aquacel hydrofiber) are better for a large amount of exudate. The middle layer should be absorbent, and the outer layer should be a charcoal dressing (e.g., Carboflex) to absorb odor. To minimize trauma to the lesion, ask the family and the nurses to change the dressings only when they are no longer absorbent or are not controlling the odor. The best way to remove them is to soak them off.

Pressure Ulcers

Pressure ulcers in terminally ill cancer patients have the same causes as those in other bed-bound patients: pressure leads to ischemia of the skin due to injury to the vascular, lymphatic, and other interstitial transportation structures. Friction, maceration, and shear forces contribute to vulnerability to pressure injury. Pressure ulcers occur most often in areas of bony prominence, especially the ischium and sacrum.

Prevention. Prevention of pressure ulcers is often possible, and your staff can educate the family in how it is done. Many visiting nurse associations and hospice programs include a physical therapist who can teach the health aides and family to provide the physical care the patient will need.

The goal is to minimize the time the patient lies or sits in one position, being particularly careful to relieve pressure over bony prominences. Multiple bed pillows can be used for the frequent repositioning. Bed cradles, elbow and heel

pads, and wheelchair cushions are all useful in an individualized plan of care. Maintaining adequate nutrition and hydration are of course helpful but not always possible in this population. Multivitamin and mineral tablets or supplemental vitamin C (1000 mg/day) and zinc (220 mg/day) can be added to the diet of those unlikely to obtain enough from food.

Of course, the chair or mattress on which the patient lies is of particular importance, especially if the patient is very old, thin, or immobile and therefore at high risk for developing pressure ulcers. It may be worthwhile to have a consultant evaluate the need for a pressure-relieving mattress. Some devices, for example, have air cells that alternately inflate and deflate. The choice of mattress will depend on the patient's needs and what the patient can afford. The AHCPR guidelines on prevention and treatment of pressure ulcers categorize the available options by efficacy. Medicare will pay for category I products for patients who have stage II to III ulcers and category II products for those with stage IV ulcers.

Therapy. As with fungating wound lesions, nursing protocols are available for the treatment of all stages of pressure ulcers; sources, including the 1994 AHCPR guideline on pressure ulcers, are given at the end of the chapter (see Bergstrom et al. 1994). Some general treatment principles are outlined below. Local care should be directed toward prevention and comfort. Topical care techniques described for fungating skin lesions can also be used for pressure ulcers in palliative care. New hope for resolution of pressure ulcers appeared in 2003 with the report of dramatic healing of grade 3 to grade 4 pressure ulcers of the foot by nerve growth factor applied directly to the ulcer (Landi et al. 2003). Terminally ill patients were excluded from this study, however.

Preventing Contamination; Minimizing Shear Forces. Polyurethane films or hydrocolloid dressings (e.g., Tegaderm, Duoderm) can be used as dressings for pressure ulcers that are neither necrotic nor infected and need only a moist environment to heal. As with dressings over fungating lesions, the caregiver or nurse should change these only when necessary.

Protecting the Wound; Promoting Healing. If the pressure ulcers are infected or have necrotic tissue, sterile normal saline irrigation is needed, and enzymatic agents (Elase, Travase, Accuzyme, Santyl [collagenase], streptokinase) can remove the eschar. As with fungating lesions, hydrocolloid dressings (Duoderm, hydrogel xeroform, Granuflex) are used if there is little exudate; alginate dressings (Kaltocarb, Kaltostat, Aquacel hydrofibers) are used if there is a large amount.

Eliminating or Controlling Infection; Debridement. Polysaccharide dextranomer granules (Debrisan) can be poured in a clean, moist wound and covered

with a semi-occlusive dressing. They will draw the bacteria and dead cells up out of the wound. Unlike the other dressings, this should be cleaned and reapplied daily until the wound is clean and appears to be healing. If odor is a problem, a charcoal dressing (Carboflex) will be needed.

Pruritus

Etiology. It was formerly thought that itch and pain were mediated by the same receptors. This turns out not to be the case. Itch-specific nerves have been found in both the peripheral and the central nervous systems (Oaklander et al. 2003). Injury to these nerves, such as occurs in herpes zoster infections—especially those of the face—can cause a pathologic itch rather than pain. Anecdotal reports of the efficacy of aprepitant offer the intriguing idea that the same NK-1 inhibitors involved in pain transmission may be involved in mediating pruritis. Patients taking aprepitant, an NK-1 inhibitor, as part of an antiemetic regimen noted marked decrease in their pruritis. Three of these patients had Sezary syndrome (Duval and Dubertret 2009), and another had begun erlotinib for non–small cell lung cancer; all had excellent symptomatic relief (Vincenzi et al. 2010). Chemical mediators of pruritus include histamine (H1, not H2, receptors) and serotonin (5-HT2 and 5-HT3 receptors). Readers interested in more speculation about the etiology of itch are referred to the discussion referenced in this chapter's bibliography (Miller 2007).

Why scratching relieves an itch is still not entirely understood, but inducing pain in the area of the itch eliminates the itching sensation. Scratching does activate myelinated A-delta sensory fibers, which temporarily stops the pruritus. Additionally, the common itching that accompanies epidural opioids arises from opioid-induced inhibition of only the pain pathways. And the pruritus that accompanies liver failure may be mediated by a similar selective blockade by endogenous opiates, because it responds to naloxone or naltrexone.

But the vast majority of pruritus in advanced-cancer patients is not due to injury of the "itch" nerves. Rather, it is caused by the same conditions and illnesses that occur in people without cancer: dry skin, allergic reactions to drugs, uremia, cholestasis, or psychological stress. In addition, the pruritus can be caused by opioids, EGFR-inhibitors, skin involvement with cancer, or a paraneoplastic process, such as is seen in patients with Hodgkin's disease and cutaneous lymphomas. Patients with myeloproliferative disorders also itch. They have increased numbers of cutaneous mast cells that can be activated by heat or other stimuli to produce pruritus.

PRACTICE POINTS: RELIEVING PRURITUS

- Patients should bathe with lukewarm water and avoid bath products containing deodorants or perfumes.
- Skin should be kept moist and fingernails short.
- Cooling or anesthetic creams may be applied.
- Oral antihistamines or NSAIDs may be needed.
- Cholestyramine, paroxetine, mirtazapine, sertraline, low-dose naltrexone or nalmefene, or methyltestosterone may be effective for cholestatic pruritus. Mirtazapine may help pruritus from other causes as well.

Patients with pruritus should keep the skin moist by frequent lubrication, cut fingernails short, and avoid all bath products that contain perfumes or deodorants. The baths themselves should be lukewarm, or oatmeal baths can be tried. Cooling the skin with menthol-containing creams (one-quarter percent menthol), camphor, peppermint, colloidal oatmeal lotions, or ice packs can provide symptomatic relief, as can calamine lotion or Caladryl (a combination of calamine lotion and Benadryl) and topical anesthetics (benzocaine, ELA-Max, EMLA). TENS machines have also been used by some patients to good effect.

Biliary Obstruction. If the pruritus results from biliary obstruction, internal stenting (Dy et al. 2012) or radiation to obstructing nodes in the porta hepatis often relieves the pruritus for as long as the patient lives. If the obstruction cannot be relieved, cholestyramine (Questran), the SSRI paroxetine (Paxil), or methyltestosterone may be effective. Sertraline reduced pruritis within days in two small trials of patients with cholestatic pruritis (Howard et al. 2012). A very low-dose naloxone infusion titrated to 0.2 mcg/kg/min followed, if no opioid withdrawal effect was noted, by oral naltrexone 12.5 to 25 mg two to three times daily(or nalmefene 5 mg) was very effective in reducing scratching activity in patients with intractable pruritis from cholestasis (Jones and Zylicz 2005). Mirtazapine, which is an H1, 5-HT2, and 5-HT3 receptor antagonist, has also been reported to relieve pruritus in patients with cholestasis, advanced Hodgkin's and non-Hodgkin's lymphomas, and renal failure (Howard et al. 2012).

Other Causes. Antihistamines (e.g., diphenhydramine [Benadryl]) will help when the cause of the itching is histamine release. Paroxetine is helpful for patients with paraneoplastic or opioid-induced pruritus. Ondansetron, a 5-HT3 receptor antagonist, is effective for opioid-induced pruritus and pruritis from myeloproliferative diseases such as polycythemia vera, but a systematic review

did not find that it had significant benefit in relieving pruritis from cholestasis or uremia (To et al. 2012). As noted above, aprepitant, an NK-1 inhibitor, has anecdotal reports of efficacy.

PRACTICE POINTS: SYMPTOMATIC THERAPY OF PRURITUS

Etiology	*Therapy*
Histamine release	Diphenhydramine
Cholestasis	Cholestyramine, paroxetine, sertraline, mirtazapine, methyltestosterone, naloxone, naltrexone, nalmefene
Paraneoplastic process	Paroxetine, mirtazapine
Opioids	Paroxetine, ondansetron, naloxone, naltrexone
Myeloproliferative process	Ondansetron
Renal failure	Ondansetron, mirtazapine

Doses: Diphenhydramine 25 to 50 mg p.o. every 8 hours; paroxetine 10 to 20 mg/day p.o.; sertraline 50 to 200 mg p.o. daily; mirtazapine 15 mg p.o. h.s.; methyltestosterone 25 mg sublingual b.i.d. for 7 to 10 days; naloxone, naltrexone, nalmefene: see text; ondansetron 8 mg p.o. b.i.d. to t.i.d.

Oral antihistamines are probably the best nonspecific relievers of pruritus, but they may cause excessive daytime sedation. If sedation occurs, try a combination of antihistamine and pseudoephedrine. NSAIDs are occasionally useful because prostaglandins at least partially mediate pruritus. Opioids, on the other hand, are not: as discussed above, they may induce pruritus. Paroxetine (Paxil), an antidepressant that is an SSRI (like fluoxetine [Prozac]), was effective in five patients with pruritus arising from various etiologies. Dosing ranged from 5 to 30 mg/day (Zylicz et al. 1998).

Insomnia

Sleep disturbances occur in 30 percent to 75 percent of cancer patients (Berger et al. 2005). Fifty-nine percent of patients who underwent curative surgery for various cancer types had insomnia when first studied prior to the surgery, and 36 percent had persistent insomnia at the time of the last follow-up, 18 months later (Savard et al. 2011). No specific type of cancer appears to have the highest

rates of sleep disturbances, but less well-educated and young patients report symptoms more often; other factors reliably related to insomnia included comorbid medical conditions, less physical activity, current use of tobacco, and more depression and fatigue (Phillips et al. 2012).

In their clinical guideline for chronic insomnia, Schutte-Rodin and colleagues (Schutte-Rodin et al. 2008) offer a set of questions that can help you obtain a comprehensive sleep history. To meet the official criteria for insomnia, a patient must have either difficulty falling asleep (i.e., taking more than 30 minutes) or difficulty staying asleep (when in bed trying to sleep, actually asleep less than 85 percent of the time) (Savard and Marin 2001). This problem must occur at least three times a week and must affect the patient's function in the daytime. Patients may have transient insomnia (lasting a month or less), short-term insomnia (one to six months), or chronic insomnia (longer than six months). Insomnia occurs in one-third to one-half of people with advanced cancer. These patients usually do not report difficulty falling asleep, but they have trouble staying asleep.

The sleeplessness can often be more troublesome to the patient's family than to the patient, but whether or not patients recognize it, lack of sleep can be contributing to their distress in many ways. At a minimum, they will feel much as we did when, as residents, we were up all night on call. But in addition, sleep deprivation may exacerbate pain and increase a patient's chance of becoming depressed.

Etiology. Patients with cancer have numerous reasons for sleepless nights. Among them are many of the problems I have already discussed—pain, depression, anxiety, delirium, dyspnea, nocturnal hypoxia, nausea and vomiting, pruritus, or hot flashes from estrogen or androgen deficiency (discussed in the next section). Medications that can cause insomnia include corticosteroids and antiemetics (prochlorperazine, metoclopramide, 5-HT3 receptor antagonists) (Savard and Marin 2001).

Patients' sleep-wake cycle may be somewhat reversed, because they are inactive and napping much of the day and then not sleepy at night. If they are severely iron deficient or uremic, are taking tricyclic antidepressants, or have a peripheral neuropathy, they may also be wakened by restless leg syndrome. For some people, very small doses of caffeine or alcohol may be enough to keep them awake at night.

Therapy. Insomnia may be treated either nonpharmacologically or with medications. When appropriate, I ask patients to consider professional counseling to explore some of the psychological, financial, and spiritual implications of their illness that are contributing to their insomnia, and to get help in resolving

them. A visit from the lawyer to finalize a will, from the hospice team to reassure the patient that his family will be supported through his final days, or from the rabbi or parish priest can often solve the problem and end the sleepless nights.

PRACTICE POINTS: NONPHARMACOLOGIC THERAPY FOR INSOMNIA

- Psychological, legal, or spiritual counseling for concerns contributing to insomnia
- Eliminating daytime naps
- Going to bed at a set time
- If awake 30 minutes later, doing some relaxing activity in or out of bed
- Instruction in biofeedback, relaxation therapy, or hypnosis

If these efforts are not sufficient, techniques developed by sleep experts for patients without cancer may be. Encourage patients not to nap during the day and to remain out of bed as long as possible. Suggest that they go to bed and get up at a set time, no matter how tired they are, and if they do not fall asleep within thirty minutes, that they engage in some relaxing activity, either out of or in bed. Progressive muscle relaxation or other forms of relaxation therapy, biofeedback, and hypnosis using imagery have been shown to be helpful as a component of short-term management, particularly for patients who cannot get to sleep or cannot regain sleep after they've awakened in the night.

Medications can alleviate insomnia when these other approaches are ineffective (Table 9.7). Data from controlled trials indicate that benzodiazepines, antidepressants, zolpidem (Ambien), and a melatonin receptor agonist, ramelteon (Rozerem), are effective agents. Melatonin itself is not. Neither was valerian, which was tested in a phase III randomized placebo-controlled double-blind study (Barton et al. 2011).

Ideally, choose an agent that specifically addresses the cause of the insomnia, such as agents for pain, anxiety, and depression discussed in Chapter 6 and earlier in this chapter. For patients who develop nighttime delirium that is keeping them and their families awake, oral quetiapine (Seroquel) is useful. For older patients, start with 25 mg at bedtime; younger patients can tolerate initial doses of 50 mg at bedtime. Olanzapine (Zyprexa) (2.5 to 5 mg p.o. at bedtime) or haloperidol (e.g., Haldol) (beginning at 0.5 to 2 mg p.o. and increasing as needed to 5 mg), given before the onset of the agitation and repeated if needed during the night, are also usually effective. For patients with restless leg syndrome, use

clonazepam 0.5 to 1 mg orally, gabapentin 100 to 300 mg orally, or pregabalin 50 to 150 mg orally.

When you cannot determine the cause of the insomnia, zolpidem 5 to 20 mg and zaleplon 5 to 20 mg help people get to sleep, while trazodone 50 to 100 mg and temazepam (Restoril) 15 to 30 mg help people stay asleep. Initial doses should be low for the older or the cachectic patient or for those taking the medication sublingually, as blood levels are higher when the drug is taken by this route. Use eszopiclone (Lunesta) 1 to 3 mg or trazodone for older patients instead of starting benzodiazepines, because older patients more frequently develop paradoxical agitation from a benzodiazepine.

Hot Flashes

Hot flashes are intermittent feelings of heat, profound sweating, and flushing of the face and chest; anxiety and palpitations may also occur (Morrow et al. 2011). Episodes last three to ten minutes.

Etiology. Women and men with either estrogen or androgen deprivation induced by cancer treatments suffer from hot flashes. Tamoxifen causes more frequent hot flash symptoms than the aromatase inhibitors. Premenopausal women receiving cytotoxic therapy are likely to experience hot flashes from early menopause. Up to 75 percent of men who undergo androgen-deprivation therapy experience hot flashes.

Therapy. Patients with mild hot flashes can try dressing in layers and using a fan. Yoga has not been convincingly shown to be helpful (Lee et al. 2009), and exercise exacerbates hot flashes, especially in overweight women, in whom it increases the core body temperature. In contrast, relaxation therapy may decrease overall symptoms, especially when used in conjunction with pharmacologic therapy (Tremblay et al. 2008).

Although estrogen and progestational agent oral therapies are effective, they are no longer used even for women without cancer because of the excessive associated risk of inducing cancer. Both venlafaxine and gabapentin are effective therapies for hot flashes. In a head-to-head trial, most patients preferred venlafaxine (37.5 mg daily for 7 days, then 75 mg daily for 21 days) to gabapentin (300 mg daily for 3 days, then 300 mg b.id. for 3 days, then 300 mg t.i.d. for 22 days) (Bordeleau et al. 2010). In other studies, Vitamin E, soy phytoestrogen, and black cohash were not effective.

Weakness and Fatigue

Fatigue is even more prevalent than pain in patients with metastatic cancer, but much less research has been done to define its pathophysiology, etiology, or effective therapy. The 2013 NCCN cancer-related fatigue treatment guidelines define fatigue as a "distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" (2013, p. FT-1). Those doing research on the epidemiology, etiology, and therapy of fatigue use a number of fatigue assessment tools. These researchers documented that half of the patients being treated for acute leukemia or non-Hodgkin's lymphoma have severe fatigue, and almost all patients receiving chemotherapy or radiotherapy (96 percent) or in the terminal phases of cancer suffer from fatigue.

The treatment guidelines include recommended screening and evaluation protocols, and separate intervention guidelines for patients under active treatment, undergoing long-term follow-up, or at the end of life. The screening guidelines are similar to those for patients with pain, which is also a subjective experience and can be validly quantified. The guidelines recommend, as for pain, assessment on a "0 to 10" scale (0 = no fatigue to 10 = worst fatigue imaginable), expert multidisciplinary evaluation, and education and training of professionals and family members. Patients who scored greater than 7 were found to have a "dramatic decrease in physical functioning" (NCCN 2013, p. MS-5). The NCCN guidelines recommend further evaluation for any patient with a fatigue level greater than 4.

Identifiable, and sometimes even reversible, causes of fatigue can be found for some patients (Table 9.8), though the mechanisms by which they produce fatigue are not known. Pain, anxiety, depression, and insomnia are important causes of generalized weakness and fatigue. Drug side effects; pulmonary, renal, hepatic, or cardiac failure; infection; under- or overactive adrenal or thyroid function; hypogonadism (Strasser et al. 2006; Fleishman et al. 2010); and certain neurologic problems—all can present as generalized weakness, and the weakness may resolve if the causes can be reversed. Anemia (see below), poor nutrition, and alcohol or substance abuse may also contribute, and, depending on the patient's stage of disease, may be reversible.

Exercise programs and cognitive-behavioral therapies have been shown to be effective for breast cancer patients while on therapy and following treatment (Mitchell et al. 2007; Duijts et al. 2011). Although data on their effectiveness in patients with advanced disease is limited, there is no reason to think they shouldn't be tried.

If no specific cause of fatigue is identified, or the therapy is ineffective, the NCCN 2013 fatigue guidelines support using the psychostimulants methylphenidate and modafinil. Long-acting methylphenidate was effective for patients with advanced disease and severe fatigue (Moraska et al. 2010) and short-acting methylphenidate is also effective in a dose-dependent manner. The most effective doses were a mean of 10 mg by day three of therapy, rising to 20 mg by day fourteen, with a range of 10 to 40 mg (Kerr et al. 2012). Modafanil (200 mg orally daily) is helpful for patients with severe, but not mild to moderate, fatigue (Pascal et al. 2010).

Eaton-Lambert Syndrome

Eaton-Lambert syndrome is a very rare complication of lung cancer that can cause weakness. Patients with this syndrome experience a sort of "reverse myasthenia": they get stronger, instead of weaker, as the day progresses. It affects the proximal muscles most prominently and sometimes remits when the cancer remits. It can persist, however, or recur. Plasma exchange, plasmapheresis, intravenous immunoglobulin (IVIG), pyridostigmine (which improves muscle contraction), and agents that promote accumulation of calcium in the nerve terminal, such as 3,4-aminopyridine, are all used, but the systematic Cochrane review from 2005 suggests the evidence favors the use of 3,4-aminopyridine and IVIG (Maddison and Newsom-Davis 2005).

Anemia

Patients whose anemia is caused only by renal insufficiency respond to erythropoiesis-stimulating agents (ESAs) (50 to 150 U/kg t.i.w.) and oral iron supplementation. Some patients with cancer or a diseased marrow (e.g., myelodysplasia) will respond to ESAs, but they are not indicated for patients undergoing myelosuppressive chemotherapies with curative intent because there is a possible risk of increased mortality and disease progression (NCCN 2014). Those patients should receive transfusions as needed.

Blood transfusion can ameliorate fatigue in patients whose hemoglobin is less than 10 g/dL (Mitchell et al. 2007). Because blood is such a scarce resource, NCCN guidelines recommend a transfusion target of 7 to 9 g/dL for asymptomatic patients with chronic anemia, who do not have acute coronary syndrome. Symptoms are defined as "including tachycardia, tachypnea, and postural hypotension," but they do not include fatigue (NCCN 2014, p. ANEM-A).

ESAs did not improve the fatigue or weakness of patients with progressive disease, but patients who are receiving palliative therapies for stable or responsive

disease may experience an improved quality of life for each gram/deciliter of increase, with the maximum effect being between 11 and 12 g/dL. The regimen is expensive and requires subcutaneous injections weekly, or every two to three weeks, of ESA dosed according to a fixed or weight-based dosing regimen, along with supplemental oral iron for optimal response, even if total body iron stores are increased.

All ESA use is associated with a significantly increased relative risk, or odds ratio, of thromboembolic phenomena of 1.48 to 1.69 (NCCN 2014, p. MS-9), and the risk is greater for hemoglobin levels greater than 10 g/dL. Patients are also at risk of developing pure red cell aplasia (NCCN 2014). Because of these increased risks, all clinicians prescribing ESAs for any indication must be registered in a REMS program and prescribe only using the REMS guidelines; patients must give their informed consent.

Metabolic Abnormalities

Cancer-related metabolic abnormalities that can present as weakness include hypercalcemia, hypomagnesemia, hyponatremia, hypokalemia, hyperglycemia, and hypoglycemia (Table 9.8).

Hypercalcemia. Hypercalcemia is a common complication of cancer. Prior to the widespread use of bisphosphonates to slow the development of metastases, it reportedly occurred in 10 to 40 percent of cancer patients at some time in the course of their illness. Now that prophylactic use of bisphosphonates may be slowing down because of the complications of long-term use, such as osteonecrosis of the jaw, the incidence of hypercalcemia may increase.

Subtle personality changes, fatigue, anorexia, or increased constipation may be the only presenting features, but many patients or their families will, on close questioning, report polyuria, nausea, increased sedation, difficulty concentrating, or symptoms typical of delirium. The severity of symptoms correlates more closely with the speed with which the hypercalcemia developed than with the absolute level of serum calcium. Mental status changes may not resolve for several weeks following normalization of serum calcium.

Hypercalcemia in patients whose disease is refractory to chemotherapy, or for whom no chemotherapy is planned, is associated with a median survival of only about one month. This grim prognosis should be taken into consideration when planning therapy for these patients; hospice care should be offered, if this has not yet been done. Treatment for symptomatic hypercalcemia can be covered by the hospice benefit.

PRACTICE POINTS: CANCER-RELATED HYPERCALCEMIA

- Patients should be monitored for subtle signs and symptoms, especially nausea, increased constipation, and mental status changes.
- Severity of symptoms correlates with speed of development of hypercalcemia, not absolute level of calcium.
- Mental status changes may not resolve for several weeks following normalization of serum calcium.
- Adequate hydration and weight-bearing activity should be encouraged.
- Initial therapy is hydration and intravenous bisphosphonate; add furosemide only after the patient is fully rehydrated.
- Patients with refractory tumors or those who do not wish to receive tumor-directed therapy should be referred to hospice. Median survival is 30 days.

Bony metastases may cause mild hypercalcemia, which can sometimes be reversed by hydrating the patient well and making sure she stays out of bed and takes in adequate amounts of salt. Activity is helpful because bone resorption from the metastases is increased when the patient is immobile, and hypercalcemia can result. Thiazide diuretics contribute to hypercalcemia and should be discontinued.

In 80 percent of cancer patients with hypercalcemia, however, parathyroid hormone–related peptide is the cause. Specific pharmacologic therapy is usually required in addition to rehydration and furosemide diuresis. Pamidronate (Aredia) (60 to 90 mg IV over 2 hours) or zoledronic acid (Zometa) (4 mg IV over 15 minutes) given in the outpatient setting will reverse hypercalcemia caused by tumor production of parathyroid hormone–related peptide or by bone metastases within 24 to 48 hours. Pamidronate is preferred for patients with renal insufficiency, but it cannot be given when the creatinine clearance falls below 30 mL/min per 1.73 m^2. A normal calcium level is often maintained for several weeks to a few months. For patients with severe hypercalcemia, adding calcitonin (4 to 8 IU/kg SQ or IV every 6 to 12 hours) speeds normalization of the calcium levels. When the calcium level is normal, additional doses of intravenous pamidronate or zoledronic acid can be given, but after several months they tend to lose their effect.

Data on the RANK-L inhibitor denosumab in treating hypercalcemia is limited, but given the frequency with which it induces hypocalcemia in patients receiving it prophylactically to prevent skeletal-related events, it would be expected

to be an effective agent in hypercalcemic patients. In fact, in one randomized phase III trial of skeletal-related effects and quality of life in more than 2,000 patients with metastatic breast cancer, patients who received denosumab (120 mg IV monthly) developed hypercalcemia only half as often as those who received zoledronic acid (4 mg IV monthly), and its onset was delayed (Martin et al. 2012). Denosumab also successfully lowered calcium levels in a myeloma patient with renal failure (Beck and de Boer 2012).

Gallium nitrate can be considered for patients who are no longer responding to any other therapy. It can be given only once and requires a five-day continuous intravenous infusion (100 to 200 mg/m^2/day) with intensive hydration. It is expensive and may cause renal damage, but it reverses the hypercalcemia in 80 percent of cases. Unfortunately, as with the other agents, the hypercalcemia will eventually recur.

Corticosteroids are effective in reversing hypercalcemia only for patients with steroid-responsive tumors, such as multiple myeloma or some lymphomas, or the very rare lymphoma that is producing 1,25-dihydroxy vitamin D.

Hypomagnesemia. This may be caused by diuretics or may persist as a residual side effect of chemotherapy with platinum derivatives. If you cannot modify the diuretic therapy, oral replacement with magnesium oxide (400 mg daily or b.i.d.) is usually effective.

Hyponatremia. In patients with lung cancer, hyponatremia is most likely due to ectopic production of antidiuretic hormone (ADH). This syndrome of inappropriate antidiuretic hormone secretion (SIADH) can be treated by fluid restriction, but for patients with advanced cancer, demeclocycline, an agent that induces pharmacologic diabetes insipidus, is effective palliative therapy (Verbalis et al. 2007). Begin with 300 mg/day twice a day, increasing to four times daily until the sodium normalizes. Maintenance doses are 600 to 1200 mg/day orally. Escalating the dose slowly minimizes the gastrointestinal toxicity, and it is otherwise well tolerated and effective.

Rarely, hyponatremia is due to Addison's disease. Metastases from some tumors (especially lung cancers) replace the adrenal gland and cause adrenocorticoid insufficiency manifested by hyponatremia and hyperkalemia. Patients taking therapeutic doses of megestrol acetate (400 mg p.o. b.i.d.) to increase their appetites can also develop adrenal insufficiency if the megestrol is not tapered. Oral hormone replacement with hydrocortisone (20 mg p.o. every morning and 10 mg p.o. every evening) plus fludrocortisone (Florinef) (0.05 to 0.15 mg p.o.) is usually adequate.

Hypokalemia. Hypokalemia may result from diuretics used to treat edema or, very rarely, from ectopic production of adrenocorticotropic hormone (ACTH).

If octreotide, which suppresses production of ectopic ACTH, is not effective, one of various agents that ablate the adrenals (i.e., aminoglutethamide, metyrapone, mitotane) can reverse the hypokalemia. Patients who undergo attempted pharmacologic adrenal ablation need careful monitoring and, if the procedure is successful, hormone replacement.

Hyperglycemia and hypoglycemia. A common complication of the high-dose corticosteroid therapy needed by patients with spinal cord or brain metastases, or of high-dose prolonged octreotide therapy, is *hyperglycemia*, which responds to standard diabetic regimens. *Hypoglycemia* resulting from insulin-producing islet cell tumors is rare, but other, non-islet cell tumors can also impair hepatic gluconeogenesis and cause hypoglycemia. One-fifth of these tumors are hepatomas, and about two-thirds are of mesenchymal origin (i.e., mesotheliomas, fibrosarcomas, leiomyosarcomas, neurofibrosarcomas, and hemangiopericytomas).

Frequent oral feedings of simple carbohydrates often help patients with insulin-producing tumors, but intravenous infusions of glucagon and/or glucose through indwelling central catheters or PICC lines may be required. For patients with large tumors of mesenchymal origin who require high-dose intravenous dextrose infusions to control their hypoglycemia, consider palliative debulking surgery.

Anorexia and Malnutrition

Anorexia is a common complication of cancer, occurring in as many as 85 percent of patients with advanced disease. If it is part of a syndrome of depression, accompanies an infection or a gastrointestinal disturbance, is from a metabolic derangement (e.g., hypercalcemia), or is a side effect of a drug that alters the taste of food (e.g., metronidazole), the anorexia may be reversible. But in many patients with advanced cancer, anorexia occurs with no definable cause. Symptomatic treatments include frequent and appetizing meals; supplements; appetite enhancers; and parenteral/enteral feeding (Table 9.8).

Dysguesia. Dysguesia is a loss of taste acuity or a distortion of taste, often induced by chemotherapy. Patients report a bitter or metallic taste from changes in the oral epithelial mucosa, as well as from drugs excreted into the saliva. Any drug can cause these alterations, but taxanes and vincristine are most problematic. Despite treatment with zinc, folic acid, alpha-lipoic acid, and B vitamins, the dysguesia can last up to two months after the last dose of chemotherapy. Patients should be advised to eat soft, moist, fatty foods that require little chewing. Salty foods are often better tolerated than sweet ones. Amifostine has not prevented the dysguesia associated with radiation therapy (Hovan et al. 2010).

Meals and Supplements. Nutritionists will explore with patients and their families ways to make meals more appealing and supply booklets containing recipes and relevant nutritional information for patients with advanced cancer; this counseling can increase caloric intake by about 500 calories a day. For example, substitutes can be offered for meat, which is often distasteful: nuts or nut butters, or protein powders added to drinks such as milkshakes or blended fruit combinations containing, for example, ice, bananas, and orange juice. Patients can be advised to eat high-calorie foods and to change to a "grazing" style, eating several small meals a day. They can take a multivitamin pill so that they can eat what they want and not worry about maintaining a "balanced diet." Some patients like nutritional supplements (e.g., Ensure, Sustacal, Resource), but others prefer the taste of some of the powdered breakfast drinks dissolved in extra-rich milk for additional calories or, for those with lactose intolerance, in lactose-reduced milk.

There is no demonstrated benefit, however, to forcing meals or intake of these high-calorie supplements. Within a month after dietary counseling, most patients have returned to their previous caloric intake.

Several medications can act as *appetite enhancers*. Megestrol acetate (Megace) (400 mg b.i.d.) can improve appetite and cause weight gain, which may be important to patients who are concerned about their appearance. It usually does not improve strength, however, because there is no increase in muscle tissue; and if the weight gain is excessive, it may even impair the patient's activity. A two-week trial is adequate; if there is no change in appetite or weight in that time, the agent can be discontinued. Chronic use of Megace can cause subclinical and, rarely, clinically apparent adrenal suppression, which manifests as adrenal insufficiency if the drug is abruptly discontinued. Taper it over a week or more, and give stress corticosteroids to patients recently withdrawn from Megace who develop a severe medical illness or are to undergo surgery.

Androgens and Selective Androgen Receptor Modulators. Oxandrolone is an oral testosterone derivative that has been shown in several nonrandomized studies to increase weight in patients with HIV/AIDS. A prospective descriptive study demonstrated that in addition to increasing body weight, patients taking oxandrolone increased their body cell mass and their lean soft tissue mass. Patients took 10 mg orally, twice daily. Average weight increases were small (e.g., weight increase of 2.6 kg ± 3 kg; lean soft tissue mass increase of 3 kg ± 2.9 kg) but statistically significant and were associated with improved quality of life (Earthman et al. 2002). A similar improvement in patients taking oxandrolone (10 mg p.o. b.i.d) was noted in an open-label study of 131 cancer patients who were losing weight. No results of randomized double-blind placebo-controlled trials have appeared since the preliminary reports in 2003 (Tchekmedyian et al.

2003). Nandrolone is an androgenic anabolic steroid that has proved effective in reversing the weight loss of patients on dialysis or patients with AIDS, but there are not enough data on patients with cancer to recommend its use.

Selective androgen receptor modulators (SARMs) are promising agents that reverse sarcopenia and increase lean muscle mass in healthy elderly men and postmenopausal women (Dalton et al. 2011). Phase III clinical trials using enobosarm to prevent muscle wasting in patients with non–small cell lung cancer are under way. Other agents that have shown promising results but are still under clinical investigation include thalidomide, selective COX-2 inhibitors, ghrelin mimetics, and olanzapine (Zyprexa/Zydis) (2.5 to 5 mg p.o. at bedtime) (Mantovani and Madeddu 2010).

In randomized double-blind crossover trials, corticosteroids (e.g., 0.75 to 1.5 mg of dexamethasone q.i.d., 5 mg of prednisone t.i.d., or 16 mg of methylprednisolone b.i.d.) improved patients' appetites and food intake for a month or even two, but at the cost of significant side effects and no increase in weight or change in nutritional status.

Dronabinol (δ-9-tetrahydrocannabinol) (2.5 to 7.5 mg t.i.d.—also available by suppository) has been particularly effective in improving the appetites of patients with AIDS, but its side-effect profile limits the population that finds it useful. A prospective uncontrolled study of patients with advanced cancer showed that appetite was improved, but almost one-quarter of the patients could not tolerate the side effects of even the lowest dose (i.e., 2.5 mg b.i.d.).

Mirtazapine (Remeron) at low doses (15 mg p.o. at bedtime) improves appetite but no data are available on whether mirtazapine produces weight gain in patients with advanced cancer.

Adenosine triphosphate (75 μg/kg IV infusion for 30 hours every 2 to 4 weeks) helped patients with stage IIIB or IV non–small cell lung cancer maintain their body composition and minimally increase their weight. The study was randomized but not blind or placebo-controlled (Agteresch et al. 2002).

Cyproheptadine and hydrazine sulfate, though initially promising, are no longer recommended. No significant increases in appetite, food intake, or weight were noted in several randomized placebo-controlled trials.

Enteral or parenteral feeding. Enteral or parenteral feeding is most useful early in the course of illness, when patients are undergoing surgery, chemotherapy, or radiation therapy. If a patient cannot eat or absorb food because of gastrointestinal disease resulting from cancer or its treatment, invasive techniques to provide nutrition are warranted, especially if the process is expected to respond to therapy.

Enteral therapy through a J-tube is usually offered to patients along with initial therapy for esophageal or gastric cancer. A meta-analysis of six randomized

trials of patients undergoing upper gastrointestinal surgery indicated that, compared with the standard formula, an immunonutrition enteral formula enriched with arginine, omega-3 fatty acids, and RNA decreased the incidence of postoperative infections and led to shorter lengths of stay (Heys et al. 1999).

Patients who are aspirating because of reversible recurrent laryngeal nerve paralysis, or whose enteral obstruction is expected to improve after specific therapy for cancer of the esophagus or the head and neck, for example, are very likely to benefit from a nasogastric feeding tube or a feeding gastrostomy or jejunostomy for several months until the paralysis or obstruction resolves. Continuous feeding (e.g., over 12 hours in the evening and while the patient sleeps) is usually well tolerated and, unlike bolus feeding, does not induce diarrhea. If diarrhea does occur, it can usually be managed by diluting the hypertonic preparations or changing to a supplement with a different formulation. The tubes are placed in the patient either in the hospital or in a short-procedure unit, and the family is taught how to use them. Often, patients can give themselves the feedings, either as bolus feedings or by continuous drip while they sleep.

Parenteral nutrition benefits selected populations (e.g., bone marrow transplant recipients and those undergoing hepatectomy for hepatocellular carcinoma) and patients with bowel obstruction who do not have cancer cachexia but who cannot use the enteral route.

Severely malnourished patients with gastrointestinal malignancies (i.e., who have lost >10 percent of their usual body weight over the 6 months prior to diagnosis) probably benefit from perioperative parenteral nutrition. A large randomized trial in gastric and colorectal cancer patients demonstrated decreased noninfectious complications and possibly decreased mortality in patients randomized to parenteral nutrition 10 days before surgery and 9 days after (Bozzetti et al. 2000). Bozzetti and colleagues recommend attention to preoperative hydration status (to minimize pulmonary complications) and prevention of hyperglycemia (to minimize infections).

Clinical practice guidelines (Mirhosseini et al. 2005) recommend that selected patients with malnutrition from refractory tumor receive parenteral nutrition. Capital Health Care (currently named Capital Caring) developed a Home Parenteral Nutrition Program Guideline for Trial of Parenteral Nutrition based on the cited clinical practice guidelines for parenteral nutrition and others (Table 9.9) (Mirhosseini et al. 2005).

Parenteral nutrition, however, is not indicated in the vast majority of cancer patients. Though many patients having parenteral nutrition will take in more calories and gain weight, routine use of parenteral nutrition does not de-

crease chemotherapy-induced complications, prolong life, or reduce perioperative morbidity or postoperative mortality (Casarett et al. 2005).

Patients with far-advanced cancer are unlikely to benefit either from a feeding tube or from parenteral nutrition. They rarely complain of hunger or thirst, and small amounts of water or food satisfy them. Nevertheless, they may ask for enteral or parenteral nutrition because they associate their lack of food or water intake with their weakness or lethargy. Unfortunately, while malnutrition can contribute to weakness, reversing malnutrition does not lead to marked increase in strength or energy in patients with extensive, refractory disease. The reasons for this are unclear.

Rarely, even after I explain this, some patients or their families are still interested in enteral or parenteral nutrition. For some families, this is because they harbor one of the hidden concerns discussed earlier: feelings of personal rejection because the patient does not want to eat; a sense that the patient has given up and will abandon them when they are not ready to let her go; or a feeling that the patient does not love them enough to continue the fight.

Others may not fully understand the implications of receiving an enteral device and being fed with tube feedings. The complications that may ensue from enteral feeding via feeding tube, gastrostomy, or jejunostomy are listed below (adapted from Ahronheim 1996).

Problems Related to the Feeding Device or Its Placement

- Discomfort
- Dislodgment
- Nasal, esophageal, gastric, or intestinal erosions or perforations
- Bleeding
- Peritonitis
- Abdominal wall leakage or cellulitis
- Ileus or bowel obstruction
- Pneumothorax
- Complications of the anesthesia required for placement
- Initiation of restraints on patient mobility

Problems Related to the Solutions Infused

- Electrolyte disturbance
- Bloating
- Regurgitation
- Aspiration
- Diarrhea

When patients and their families understand both the limited benefits and the magnitude of the problems enteral feeding can cause, it becomes much less attractive.

Parenteral feeding is likewise fraught with complications both during catheter insertion (e.g., pneumothorax, hemorrhage) and later (e.g., bacterial and fungal infections, catheter occlusion and migration leading to superior vena cava syndrome). As I reviewed in Chapter 4, palliative care practitioners can partner with you to help these patients and families weigh the benefits and burdens of artificial nutrition. When in doubt, a time-limited trial may be helpful to determine whether artificial nutrition remains effective in enabling patients and families to achieve their goals.

Coping Strategies

When the weakness is not reversible, it is useful to give the patient and his family some strategies for dealing with it. Patients may mistakenly think that going to bed for a time will help them regain their normal strength, as it did in the past when they had another illness. Advise them to minimize the time they spend in bed so as to maximize their remaining strength. Selected patients may benefit from physical therapy consultation.

PRACTICE POINTS: HELPING PATIENTS COPE WITH WEAKNESS AND FATIGUE

- Encourage patients to spend time out of bed.
- Advise patients to obtain equipment that will help them maintain mobility.
- Encourage patients to continue the activities that are most important and to relinquish others.
- Encourage sensory, intellectual, and interpersonal stimulation.
- Provide emotional support to family members who are distressed by the patient's symptoms.

Patients can maintain mobility by renting the portable equipment that is available: walkers, wheelchairs, lift chairs, electric hospital beds, tray tables, and commodes or shower chairs. Many insurance companies cover these rentals, and eligible veterans can use them free of charge.

Common sense advice like planning for short rest periods during the day, limiting trips, and delegating exhausting chores can be surprisingly helpful. It is

often hard for people to relinquish these tasks, especially if the tasks helped define their role in the family. You or your staff can often assist patients in identifying which of these tasks are most important to them and which they wouldn't mind delegating: cooking, for example, may be more important than shopping; reading the bedtime story may be as satisfying as giving the nighttime bath.

For those who are bedridden, sensory, intellectual, or interpersonal stimulation is still important. Listening to music, reading, or drawing can be encouraged. Or you can urge the family to take out of the library, rent, or purchase audiobooks or DVDs, or encourage other family members or friends or hospice volunteers to drop by to reminisce, play games, or read to the patient.

A friend of mine was even more imaginative. One Saturday, she turned her mother's hospital room into a picnic site, complete with a hamper and Italian delicacies. On another occasion, for a holiday meal, she brought formal linens and tableware and arranged a Skype call on her computer so her mother could join the rest of the family in the festivities.

It helps me to remember that, in most cases, the weakness is not troublesome to the patient, who is often living a very satisfying life despite what others may see as disabling limitations. Families are much more likely to be suffering because of the changes in the patient than is the patient himself. The family members are often the most in need of our help.

Role of Hospice Programs

Hospice programs are often the answer. Patients in hospitals, nursing homes, or inpatient hospice facilities have 24-hour nursing and physician coverage to help alleviate their symptoms. But many patients prefer and are able to be cared for, and to die, at home. Their families, who provide much of their care, often find this a particularly difficult time. Families of patients dying of cancer share a number of needs (Cherny et al. 1996). They include:

- Comfort for the patient
- Information and communication
- Evaluation of the family's needs and resources
- Education about care
- Emergency provisions
- Review of how the family is coping
- Care of the family when the patient is unconscious
- Preparation of the family for the dying process
- Conflict resolution

The members of a hospice team can help you meet all these needs. Hospice nurses, social workers, chaplains, and volunteers are superb problem solvers who have developed detailed strategies that are usually effective in addressing the complex sources of distress of patients with advanced cancer. As I discussed in Chapter 4, hospice teams anticipate family concerns and analyze and develop solutions for patients' and families' psychological, social, financial, and spiritual needs. Medical and nursing care are also expertly delivered. While you continue to approve the orders, nurses and social workers from the team make the needed assessments, and they educate the family in techniques of care and ensure that the appropriate medications, supplies, and services are obtained to provide optimal patient comfort.

Hospice nurses make routine home visits as often as needed and are a source of information and of communication from the family to you or other caregivers. Some patients require only weekly visits from them; others may need a nurse daily; and a few will need 24-hour nursing, and for those patients who need them, the nurses will also authorize up to two hours a day of home health aide services. Nurses bring medications and supplies, including emergency provisions, prepare the family for the dying process, and help support the family if the patient becomes unconscious.

Hospice programs have nurses available by phone 24 hours a day, and a nurse will make a home visit at any time for emergencies. Hospice nurses can serve the very important role of being with the family at the bedside as the patient dies, adjusting the patient's medications, and reassuring the family that everything possible is being done; they will also talk with the family immediately after the death to offer comfort and to assess and attempt to alleviate any persistent concerns.

The Medicare hospice benefit pays for all these services: personnel, medications, durable medical equipment, supplies, and any other authorized services needed to provide patient comfort (e.g., a surgical consultation to debride a wound). Some people are reluctant to elect this benefit because they misunderstand several of its provisions. For example, patients may think they have to give up their private physician. That is not true: patients can continue to see you; you are allowed to bill for professional services separately under Medicare Part B, as before.

And patients can be hospitalized if they develop a problem requiring an inpatient stay for management of a symptom, such as rapidly escalating pain or severe delirium. Hospice programs are required to offer four levels of care: routine home care, continuous home care (24-hour nursing), respite care, and inpatient care. They have contracts with local hospitals so that they can provide continuous care at whatever site the patient requires it.

Hospice services are also available to patients without the Medicare hospice benefit. Private insurance, managed care plans, and Medicaid programs offer various hospice benefits, and the indigent will be cared for as well. Your local hospice agencies, some of which are nonprofit, others for-profit, will be happy to inform you of the range of services they can provide. If you have other questions, contact the National Hospice and Palliative Care Organization (NHPCO, www.nhpco.org).

Role of the Palliative Care Team

Unlike hospice teams, palliative care teams can help patients and families from the onset of the cancer diagnosis. Palliative care teams address all the domains of distress of patients with cancer and their families, as do hospice teams. As CAPC, the Center to Advance Palliative Care, explains,

> Palliative care is specialized medical care for people with serious illnesses. This type of care is focused on providing patients with relief from the symptoms, pain, and stress of a serious illness. The goal is to improve quality of life for both the patient and the family.
>
> Palliative care is provided by a team of doctors, nurses, and other specialists who work with a patient's other doctors to provide an extra layer of support. Palliative care is appropriate at any age and at any stage in a serious illness, and can be provided together with curative treatment.

Palliative care teams almost always include nurses (usually nurse practitioners) and physicians (Billings and Pantilat 2001), and some also include social workers, chaplains, pharmacists, bereavement counselors, and volunteers (Billings and Pantilat 2001; Ng and von Gunten 1998). These multidisciplinary or interdisciplinary teams offer assessment and management of physical, psychological, social, and spiritual causes of distress, patient and family education, and counseling, problem solving, and support for the family. If you don't have an oncology social worker as part of your team, the palliative care team's social worker can be of particular help to you.

Reports on the efficacy of palliative care teams are mostly from uncontrolled studies, but they do indicate positive effects on patients' physical symptoms and quality of life, improved family satisfaction, and decreased hospital costs and resource utilization (Gazelle et al. 2001; Manfredi et al. 2000; Smith et al. 2003; Swetz and Kamal 2012). A systematic quantitative review of the impact of palliative care teams on the end-of-life experiences of patients and their families found evidence for a small benefit; the benefit of team care was

strongest when the team was working with patients in their homes (Higginson et al. 2003).

Integration of Oncology and Palliative Care

It is time for oncology and palliative care to collaborate in the care of their patients, especially those patients with advanced disease undergoing treatment and patients who would qualify for a hospice program but do not feel "ready" for one, or who have become accustomed to an intensity of supportive care (e.g., total parenteral nutrition or transfusions) that they or their family feel contributes significantly to their quality of life (Smith et al. 2012; Gilligan 2003; Abernathy and Currow 2011; Abrahm 2012). These services may not be available from local hospice programs because those programs receive about $160 per day per patient to provide all the services, medications, and equipment described above.

The NCCN guideline for palliative care (2013) and the ASCO vision for 2020 (Ferris et al. 2009) both recommend early consults for selected cancer patients. Patients with advanced disease may even live longer, as well as having less depression and a better quality of life, as did the patients studied who had advanced lung cancer (Temel et al. 2010).

In 2000, a survey of 100 U.S. teaching hospitals revealed that only 18 percent had a palliative care consultation service, and 19 percent had an inpatient unit (Billings and Pantilat 2001). As of 2011, however, more than 1,900 hospitals throughout the United States had palliative care teams. Although it is not a requirement for the designation, all NCI-designated comprehensive cancer centers now have palliative care teams (Debono 2011), as do at least 78 percent of non-NCI–designated facilities caring for cancer patients (Hui et al. 2010), including most of those housing oncology fellowship programs.

Palliative care teams work with patients at any point along their disease trajectory (diagnosis, relapse, or terminal care). They can provide both consultation and primary clinical care. Most teams are hospital based, but more and more are providing care to outpatients in physicians' offices, in home consultations, or in concert with a hospice run by the same organization (Billings and Pantilat 2001; Gazelle et al. 2001; Nelson and Walsh 2003). Reviews of the literature on the financial, operational, and systemic barriers and workforce limitations to successful early integration of palliative care or hospice programs into the care of oncology patients are provided in the bibliography at the end of this chapter, and they provide a number of model systems that have overcome these barriers.

Benefits of integration to the oncology team. The palliative care team can be a useful partner to your team in both the inpatient and the outpatient setting.

Members of the team can get to know your patients and their families early in the course of their disease if you bring them in to help you manage a difficult symptom. After working with your patients over weeks to months, the palliative care team members will more easily assist your team during difficult family meetings. They can remain in the room after you have left to see another patient, to answer questions that the patient or family may have forgotten or may be reluctant to ask you.

Palliative care team members can be there, as well, if you have to break "really bad" news, recommend stopping chemotherapy, discuss hospice care, or explore goals and values so as to help your patients and their families determine their wishes regarding resuscitation. Also important is the support the palliative care team can offer you and your staff in dealing with the emotional toll these situations exact. The palliative care team can even arrange services of remembrance to help acknowledge and process the grief associated with this work.

Institutional benefits. Finally, palliative care teams benefit the institutions within which they work, helping to increase staff morale, decrease staff turnover, and enhance staff expertise in palliative and end-of-life care. Palliative care teams based in academic medical centers and in teaching hospitals affiliated with these centers also provide training and perform research in palliative medicine (von Gunten 2002). Both through consultations and through formal and informal didactic sessions, palliative care teams offer education about the palliative care needs of patients undergoing active therapies, as well as offering insight into the stresses of patients and families as they make the transition to care without chemotherapy (Abrahm 2000; Oneshuck et al. 1997; Sheldon and Smith 1996; von Gunten et al. 1995).

In palliative care teaching rounds and seminars, medical students, residents, and fellows learn how to work within an interdisciplinary group and how to provide comprehensive care across care sites (inpatient, outpatient, home). The teams collaborate in joint problem solving to arrive at integrated solutions, a practice not often observed in standard medical training (Beninghof and Singer 1992; Billings and Block 1997; Boaden and Leaviss 2000; Browne et al. 1995; James and MacLeod 1993; Nash and Hoy 1993). This instruction can remedy the deficits of a medical education and training that leave clinicians ill-prepared to alleviate the suffering of patients with advanced disease, or of their families (Billings and Block 1997; Ferrell et al. 1999; Abrahm 2012).

Summary

In this chapter I have reviewed the major problem areas affecting patients with far-advanced cancer: anxiety, depression, and personality disorders; xerostomia, infections and other lesions of the oral cavity; ascites, diarrhea, dysphagia, nausea, vomiting, and bowel obstruction; dyspnea, cough, hemoptysis, and hiccups; therapy- or cancer-induced skin problems; sleeplessness; hot flashes; and weakness and fatigue.

Patients with far-advanced cancer can experience many of these distressing symptoms. The causes of these problems can often be reversed, even in very frail patients. When we cannot reverse the cause of the problem, there is usually an effective symptomatic treatment available. Collaborating with palliative care teams and hospice programs can enhance your ability to provide comfort and quality of life to your patients and their families, at the beginning of treatment and when the disease advances.

Tables

Tables 9.1 to 9.9 follow on pages 496–507.

Table 9.1 Pharmacologic Treatment of Anxiety and Depression

Class/Drug	*Dose*	*Comments*
ANXIETY		
Benzodiazepines		
Lorazepam (Ativan)	0.5–2 mg q1–4h max 10 mg / 24 hr	Tablets, sublingual tabs, and liquid available; tablets can be used p.r.
Clonazepam (Klonopin)	0.5–1 mg p.o.	Can be given h.s., or up to t.i.d.; tablets have been used p.r. Do not exceed 4 mg / 24 hr.
Alprazolam (Xanax)	0.25–2 mg p.o. t.i.d.	Severe "rebound" effect; not recommended for chronic use.
Diazepam (Valium)	5–10 mg p.r. h.s.	Useful for patients unable to take oral medication.
Oxazepam (Serax)	15–30 mg p.o. h.s.	For insomnia from anxiety.
Temazepam (Restoril)	7.5–30 mg p.o. h.s.	For insomnia from anxiety.
Zolpidem (Ambien)	5–10 mg p.o. h.s.	For insomnia from anxiety.

Class/Drug	*Dose*	*Comments*
AKATHISIA		Discontinue metoclopramide, haloperidol, or other typical or atypical antipsychotic agents.
Propranolol	40 mg p.o. t.i.d.	Metoprolol IV can also be used.
Mirtazapine	7.5–15 mg p.o. daily	
Zolmitriptan	7.5 mg p.o. daily	
DEPRESSION		
Selective serotonin reuptake inhibitors (SSRIs)		
Citalopram (Celexa)	20–40 mg p.o. h.s.	May cause minimal sexual dysfunction.
		Prolongs QTc at high doses.
Escitalopram (Lexapro)	10–20 mg p.o. h.s.	May cause minimal sexual dysfunction.
		Prolongs QTc at high doses.
Sertraline (Zoloft)	50–200 mg p.o.	Likely to have drug-drug interactions.
Paroxetine (Paxil)	20–60 mg p.o. h.s.	Sedating; can be difficult to discontinue; very likely to have drug interactions.
Fluoxetine (Prozac)	20–80 mg/day p.o.	Stimulating; causes anorexia; very likely to have drug interactions.
Fluvoxamine (Luvox)	25–200 mg p.o. h.s.	Very likely to have drug interactions.
Serotonin and norepinephrine reuptake inhibitors (SNRIs)		
Venlafaxine (Effexor)	75–225 mg p.o.	Used alone or added to SSRI. Must be tapered off.
Venlafaxine extended release (Effexor XR or Venlafaxine ER)	37.5–100 mg p.o. daily or b.i.d.	Used alone or added to SSRI. Must be tapered off.
Duloxetine	10–20 mg p.o. daily or b.i.d.; maximum 20–60 qd or b.i.d.	
Psychostimulants		May be used with another class of antidepressant (e.g., SSRI).

(continued)

Table 9.1 Pharmacologic Treatment of Anxiety and Depression *(continued)*

Class/Drug	*Dose*	*Comments*
Methylphenidate (Ritalin)	5–60 mg p.o.	Divided doses (8 a.m., noon).
Dextroamphetamine (Dexedrine)	5–60 mg p.o.	Divided doses (8 a.m., noon).
Others		
Clorazepate (Tranxene)	15–60 mg/day p.o.	For anxiety from alcohol withdrawal.
Mirtazapine (Remeron)	15–45 mg p.o. h.s.	Also enhances appetite and decreases nausea.
Bupropion (Wellbutrin)	100 mg p.o. daily; 450 mg p.o. in 4 divided doses	Activating; can be added to SSRI or SNRIs.
Buproprion extended release (Wellbutrin XL)	150–300 mg p.o. daily	
Trazodone (Desyrel)	50–400 mg p.o. h.s.	Sedating. May prolong QTc.
Tricyclic antidepressants		
Amitriptyline, doxepin, clomipramine, desipramine, nortriptyline	10–25 mg/day p.o. h.s	Increase to therapeutic dose (50–150 mg in divided doses). Very likely to have drug interactions; may prolong QTc.

Table 9.2 Oral Care

Problem	*Therapy*
Routine maintenance	Multivitamins/minerals Brushing, flossing Antibacterial rinses (sans alcohol)
Candida	Troches (miconazole, clotrimazole), q.i.d. Ketoconazole (Nizoral), 200 mg b.i.d. p.o. Fluconazole (Diflucan), 200 mg p.o. day 1, then 100 mg/day p.o. Itraconazole (Sporanox) (tablet or solution), 100–200 mg/day p.o. Amphotericin B solution (100 mg/ml), 1 ml t.i.d. to q.i.d., rinse and spit
Xerostomia	Sugar-free sour candies Lubricants, saliva substitutes Pilocarpine (Salagen), 5–10 mg t.i.d. p.o. Cevimeline (Evoxac), 30 mg p.o. t.i.d.; bethanecol Acupuncture

Table 9.3 Pharmacologic Treatment of Nausea and Vomiting

Etiology of Nausea	*Drug*	*Dose*
KNOWN ETIOLOGY		
Initiation of opioid therapy	Prochlorperazine (Compazine)	10 mg p.o. t.i.d. to q.i.d. or 25 mg b.i.d. p.r.
	Ondansetron (Zofran)	1–4 mg p.o. t.i.d.
Vertigo	Hyoscyamine (Levsin)	1–2 tsp. (elixir) or 1–2 tablets p.o. / sublingual / chewed q4h
	Scopolamine (Transderm Scōp)	1 patch q72h
	Meclizine (Bonine, Antivert)	25–50 mg t.i.d. p.o.
Gastric acidity	Proton pump inhibitors (e.g., esomeprazole)	20 mg daily to b.i.d. p.o.
	H2 blockers (e.g., famotidine)	300 mg b.i.d. p.o. (H2 blockers may cause delirium in elderly patients)
Delayed gastric emptying	Metoclopramide (Reglan)	10–20 mg b.i.d. to q.i.d. p.o. or 1–5 mg / hr IV or SQ
	Haloperidol (Haldol)	0.5–1 mg t.i.d. p.o., p.r., or SQ
Uremia, liver metastases	Prochlorperazine (Compazine)	5–10 mg p.o. q4–6h or 25 mg p.r. b.i.d. or t.i.d.
Brain metastases	Dexamethasone	10 mg q.i.d. or 40 mg every morning p.o., p.r., or SQ
Anxiety	Lorazepam (Ativan)	0.5 to 2 mg q4–6h p.o. or sublingual
Bowel obstruction	Dexamethasone, +	10 mg IV or SQ b.i.d.
	Hyoscyamine (Levsin)	1–2 tsp. (elixir) or 1–2 tablets p.o. / sublingual / chewed q4h
	or	
	Scopolamine (Transderm Scōp) or	1 patch q72h
	Glycopyrrolate	0.2 to 0.4 mg IV q4h
	Metoclopramide (Reglan)	10 mg p.o. / SQ / IV q6h if partial bowel obstruction
Refractory bowel obstruction	Dexamethasone +	10 mg IV or SQ b.i.d. +
	Octreotide (Sandostatin)	100–200 mcg SQ b.i.d. to t.i.d.
UNKNOWN ETIOLOGY		
	Metoclopramide (Reglan) +	10 mg p.o. / SQ / IV q6h or 1 hr before meals +
	Dexamethasone	4 mg p.o., IV or SQ b.i.d.
Refractory nausea	Dexamethasone +	4 mg p.o., IV or SQ, b.i.d. +
	Olanzapine (Zyprexa, Zydis)	2.5–5 mg p.o. / sublingual q.h.s. to q.i.d.

(continued)

Table 9.3 Pharmacologic Treatment of Nausea and Vomiting *(continued)*

Etiology of Nausea	*Drug*	*Dose*
Nausea still refractory	Ondansetron (Zofran) Granisetron (Kytril) Haloperidol (Haldol)	4–8 mg b.i.d. or t.i.d. p.o. or IV 1 mg b.i.d. p.o. or IV 1–2 mg p.o. t.i.d. to q.i.d., 2–10 mg IV b.i.d. to t.i.d.
Other	Tetrahydrocannabinol (e.g., Marinol) Integrative therapies: hypnosis, acupuncture, mindfulness-based stress reduction	2.5–10 mg p.o. b.i.d. to t.i.d. (titrate to effect) See Chapter 7

Table 9.4 Emetogenic Potential of Intravenous Chemotherapeutic Agents

High (>90% frequency of emesis)	
Carmustine (>250 mg/m^2)	Doxorubicin (>60 mg/m^2)
Cisplatin (≥50 mg/m^2)	Epirubicin (>90 mg/m^2)
Cyclophosphamide (>1500 mg/m^2)	Ifosfamide (≥10 g/m^2)
Dacarbazine (>500 mg/m^2)	Streptozocin
AC combination (either doxorubicin or epirubicin with cyclophosphamide)	Mechlorethamine
Moderate (30–90% frequency of emesis)	
Aldesleukin (>12–15 million IU/m^2)	Dactinomycin
Amifostine (>300 mg/m^2)	Daunorubicin
Arsenic trioxide	Doxorubicin (≤60 mg/m^2)
Azaciditine	Epirubicin (≤90 mg/m^2)
Bendamustine	Idarubicin
Busulfan	Ifosfamide (<10 g/m^2)
Carboplatin	Interferon alfa (≥10 million IU/m^2)
Carmustine (≤250 mg/m^2)	Irinotecan
Cisplatin (<50 mg/m^2)	Melphalan
Clofarabine	Methotrexate (≥250 mg/m^2)
Cyclophosphamide (≤1500 mg/m^2)	Oxaliplain
Cytarabine (>200 mg/m^2)	Temozolomide
Low (10–30% frequency of emesis)	
Amifostine (≤300 mg)	Ixabepilone
Aldesleukin (IL-2) (≤12 million IU/m^2)	Methotrexate (>50 mg/m^2 <250 mg/m^2)
Cabazitaxel	Mitomycin

Table 9.4 Emetogenic Potential of Intravenous Chemotherapeutic Agents *(continued)*

Cytarabine (100–200 mg/m^2)	Mitoxantrone
Docetaxel	Paclitaxel
Doxoruicin (liposomal)	Paclitaxel albumin
Eribulin	Pemetrexed
Etoposide	Pentostatin
Fluorouracil	Pralatrexate
Floxuridine	Romidepsin
Gemcitabine	Thiotepa
Interferon alfa (>5<10 million IU/m^2)	Topotecan
Minimal (<10% frequency of emesis)	
Alemtuzumab	Methotrexate (<50 mg/m^2)
Asparaginase	Nelarabine
Bevacizumab	Ofatumumab
Bleomycin	Panitumumab
Bortezomib	Pegaspargase
Cetuximab	Peginteferon
Cladribine (2-chlorodeoxyadenosine)	Rituximab
Cytarabine (<100 mg/m^2)	Temsirolimus
Decitabine	Trastuzumab
Denileukin diftitox	Valrubicin
Dexrazoxane	Vinblastine
Fludarabine	Vincristine
Interferon alpha (<5 million IU/m^2)	Vinorelbine
Ipilimumab	

Table 9.5 Emetogenic Potential of Oral Chemotherapeutic Agents

Moderate to high	
Altretamine	Etoposide
Busulfan (≥4 mg/day)	Lomustine (single day)
Cyclophosphamide (≥100 mg/m^2/day)	Procarbazine
Estramustine	Temozolomide (>75 mg/m^2/day)
Minimal to low	
Bexarotene	Melphalan
Busulfan (<4 mg/day)	Mercaptopurine
Capecitabine	Nilotinib
Chlorambucil	Pazopanib
Cyclophosphamide (<100 mg/m^2/day)	Sorafenib
Dasatinib	Sunitinib
Erlotinib	Temozolomide (<75 mg/m^2/day)
Everolimus	Thalidomide
Fludarabine	Thioguanine
Gefitinib	Topotecan
Hydroxyurea	Tretinoin
Imatinib	Vandetanib
Lapatinib	Vorinostat
Lenalinomide	

Source: National Comprehensive Cancer Network (NCCN), *NCCN Antiemesis Practice Guidelines*, version 1.2013, www.nccn.org, 2013.

Table 9.6 Symptomatic Treatment of Dyspnea, Cough, and Hiccups

Cause	*Drug*	*Dose*
Dyspnea from anxiety/ panic	Lorazepam (Ativan)	0.5–2 mg p.o. or sublingual q4–6h
	Clonazepam (Klonopin)	0.5–1 mg p.o. h.s. or b.i.d.
	Midazolam (Versed)	0.2–0.5 mg IV slowly or 0.1–3 mg/hr SQ
	Morphine[1]	5–10 mg IV, p.o., or by nebulizer
	Chlorpromazine (Thorazine)	25 mg p.o., p.r., or IV
Dyspnea—other etiology	Morphine[1]	15 mg q4h p.o. or SQ; titrate upward as needed
	Integrative therapies (e.g., hypnosis, relaxation, guided imagery)	See Chapter 7.
Cough	Benzonatate (Tessalon Perles or capsules)	1–2 perles or capsules t.i.d. p.o. p.r.n.
	Dextromethorphan elixir	15–30 ml q6h p.o. p.r.n.
	Hyoscyamine (Levsin)	1–2 ml (drops) or 1–2 tablets p.o. / sublingual / chewed q4h
	Glycopyrrolate (Robinul)	0.1–0.2 mg IV t.i.d. to q.i.d.
	Scopolamine (Transderm Scōp)	1–3 patches q72h
	Morphine[1]	5–20 mg q4h p.o.
	Albuterol	0.5 mg in 2.5 mg normal saline
	Nebulized lidocaine	2 ml of 2% lidocaine in 1 ml of normal saline, for 10 min
Hiccups	Metoclopramide (Reglan)	5–10 mg t.i.d. or q.i.d. p.o., p.r., or 10 mg q4h IV Amantadine for gastro-paresis-related hiccups in Parkinson's disease
	Baclofen (Lioresal)	5–10 mg p.o. b.i.d. to 20 mg t.i.d.
	Gabapentin (Neurontin)	300 mg p.o. daily to 1200 mg daily in divided doses (usually t.i.d.). If not effective, try pregabalin 50 mg p.o. t.i.d. to 150 mg p.o. t.i.d.

(continued)

Table 9.6 Symptomatic Treatment of Dyspnea, Cough, and Hiccups *(continued)*

Cause	*Drug*	*Dose*
	Chlorpromazine (Thorazine)	25–50 mg IV once; then 25–50 mg t.i.d. p.o. or p.r.
	Haloperidol (Haldol)	2–10 mg/day p.o. p.r., or 0.5–2 mg IV q4h
	Proton pump inhibitors	Doses variable; for hiccups from GERD
	Sertraline	50–100 mg/day p.o.
	Nifedipine	10–20 mg p.o. t.i.d.

[1]Other opioids may be substituted for morphine. Begin with equipotent dose of the other opioid and titrate to effect. For patients who develop bronchospasm from morphine or related opioids, use fentanyl instead.

Table 9.7 Pharmacologic Treatment of Insomnia

Cause	*Drug*	*Dose*
Anxiety/depression		
Anxiety	Lorazepam (Ativan)	0.5–2 mg p.o. h.s.
	Clonazepam	0.5–1 mg p.o. h.s.
Depression		
Tricyclics	Amitriptyline (Elavil)	10–150 mg p.o. h.s.
	Doxepin (Sinequan)	75–150 mg p.o. h.s.
	Nortriptyline (Pamelor)	10–150 mg p.o. h.s.
	Trimipramine (Surmontil)	25–100 mg p.o. h.s.
Other	Trazodone (Desyrel)	50–150 mg p.o. h.s.
Delirium	Haloperidol (Haldol)	0.5–2 mg p.o. up to 5 mg p.o. in p.m.
	Olanzapine (Zyprexa)	2.5–5 mg p.o. h.s.
	Quetiapine (Seroquel)	25–50 mg p.o. h.s.; titrate to effect to 200 mg.
Menopausal symptoms	Venlafaxine (Effexor)	37.5–75 p.o. b.i.d.
Restless leg syndrome		
Idiopathic	*Dopamine agonists*	
	Cabergoline (Dostinex)	0.25 twice a week p.o; increase as tolerated / needed to 1 mg twice a week p.o.
	Levodopa-carbidopa (Sinemet)	25–100 mg; 1–2 tabs p.o. h.s.
	Pramipexole (Mirapex)	0.125 mg/day p.o.; increase by 0.125 mg q. 2–3 days as needed.
Painful	Gabapentin (Neurontin)	100–300 mg p.o. h.s.
	Pregabalin (Lyrica)	50–150 mg p.o. h.s.
Other	Clonazepam (Klonopin)	0.5–1 mg p.o. h.s.
UNKNOWN		
Melatonin receptor agonist	Ramelteon (Rozerem)	8 mg p.o. h.s.
Other	Estazolam (ProSom)	0.5–2 mg p.o. h.s.
	Quazepam (Doral)	7.5–15 mg p.o. h.s.
	Temazepam (Restoril)	7.5–30 mg p.o. h.s. (to maintain sleep)
	Trazadone (Desyrel)	50–100 mg p.o. h.s. (to maintain sleep)
	Zaleplon (Sonata)	5–20 mg p.o. h.s. (to initiate sleep)
	Zolpidem (Ambien)	5–20 mg p.o. h.s. (to initiate sleep)
Older patients	Eszopiclone (Lunesta)	1–3 mg p.o. h.s.
	Trazadone (Desyrel)	50–100 mg p.o. h.s.

Sources: C. J. Early, Restless leg syndrome, *New England Journal of Medicine,* 348:2103–2109, 2003; S. H. Tariq and S. Pulisetty, Pharmacotherapy for insomnia, *Clin Geriatr Med*, 24:93–105, 2008.

Table 9.8 Treatment of Weakness and Fatigue

Cause	*Drug/Procedure*	*Dose*
Anemia	Transfuse	
Renal failure	Erythropoietin (Epogen) + iron	50–150 U / kg SQ t.i.w.
Cancer / treatment related	Erythropoietin (Procrit) + iron	40,000–60,000 U SQ q. week
	Darbepoetin-α (Aranesp) + iron	200–300 µg q2wk SQ
Hypercalcemia	Pamidronate (Aredia)	60–90 mg IV over 2 hr
	Zoledronic acid (Zometa)	4 mg IV over 15 min
	Calcitonin	4–8 IU/kg SQ or IM q6–12h
	Gallium nitrate	100–200 mg/m^2/day IV over 5 days
Hyponatremia		
SIADH	Demeclocycline (Declomycin)	300 mg p.o. b.i.d. to q.i.d. until Na^+ normal; 600–900 mg / 24 hr p.o. maintenance
Adrenal replacement with tumor	Hydrocortisone +	20 mg every morning, 10 mg every evening +
	fludrocortisone (Florinef)	0.05–0.15 mg/day p.o.
Hypokalemia from ectopic ACTH	Octreotide (Sandostatin)	100–500 µg b.i.d. SQ
	Aminoglutethimide (Cytadren)	Consult with oncologist/ endocrinologist
	Metyrapone	
	Mitotane (Lysodren)	
Hypoglycemia		
Insulinoma	Glucagon	Consult with endocrinologist
Mesenchymal tumors	Debulking surgery	
Anorexia		
Dysguesia	Taxanes and vincristine cause most often	Salty, soft, moist foods requiring minimal chewing
General	Adjust diet/supplements	
	Megestrol acetate (Megace)	400 mg b.i.d. p.o.
Corticosteroids (increase appetite but not weight)	Dexamethasone	0.75–1.5 mg q.i.d. p.o., IV
	Prednisone	5 mg t.i.d. p.o.
	Methylprednisolone	16 mg b.i.d. p.o.
Other	Dronabinol (Marinol) (δ-9-tetrahydrocannabinol)	2.5–7.5 mg t.i.d. p.o.
	Olanzapine	2.5–5 mg h.s. p.o.
Anorexia and depression	Mirtazapine (Remeron)	15 mg qhs
	Methylphenidate	2.5–10 mg p.o. 8 a.m. and noon

Table 9.9 Capital Caring Home Parenteral Nutrition Program Guidelines for Trial of Parenteral Nutrition

Nutritional Criteria

1. Potential benefit from parenteral nutrition (i.e., in case of bowel obstruction, short bowel syndrome, or malabsorption), where it seems probable that death by starvation or malnutrition would ensue much earlier than death from disease progression, and enteral nutrition is not an option
2. A life expectancy in the order of months and a duration of parenteral nutrition treatment expected to be at least 6 weeks
3. High quality of life
4. Sufficient functional status and home environment for parenteral nutrition to be successfully instituted and monitored:
   —The patient's problems should be manageable at home or with the support of an outpatient program.
   —The patient's physical function should be sufficient as reflected by a Karnofsky score of greater than 50.
   —There is a family member or other person who is willing and able to assist in care.
   —The patient can be easily monitored for clinical follow-up and laboratory investigations.
   —The patient and family must be cognitively and psychologically capable of administering parenteral nutrition at home.
   —The home environment is safe, clean, and free of hazards.

Source: Adapted from N. Mirhosseini, R. L. Fainsinger, and V. Baracos, Parenteral nutrition in advanced cancer: indications and clinical practice guidelines, *J Pall Med* 8:914–918, 2005; includes references to other clinical practice guidelines for parenteral nutrition.

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CHAPTER 10

The Last Days . . . and the Bereaved

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- Components of Care of the Dying
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The Dying Patient

The last few days of life pose special problems for cancer patients, their families, and even the physicians caring for them. General practitioners, for example, have been found to suffer from "the end of the doctor-patient relationship, feelings of uselessness and failure, increased awareness of their own mortality, and the presence of 'questions without answers'" (Schaerer 1993). And taking care of dying patients is a major contributor to burnout among medical oncologists (Whippen and Canellos 1991; Jackson et al. 2008). Oncologists who saw both a biomedical

and a psychosocial role for themselves, however, who felt skilled in communicating with dying patients, and who obtained support from colleagues were more satisfied with the care they delivered and seemed to be protected from burnout. Significantly, they were the more experienced clinicians (Jackson et al. 2008).

If you are a younger clinician and have never before cared for a dying patient, you may not realize that you can get the support you need to help these patients and their families from your oncology mentors or from a palliative care or hospice team member. You might feel you have nothing to offer. But that is far from the truth. Both the patient, if awake, and the family will welcome your calls or visits and your ongoing involvement in their care. Don't worry about being blamed for what is happening, and let your instincts guide you in offering the patient and the family the respect and comfort you want to give them.

Components of Care

What do patients feel they need for a "good death"? Many patients would say:

- Physical comfort
- Maintaining a sense of continuity with one's self
- Maintaining and enhancing relationships
- Making meaning of one's life and death
- Achieving a sense of control
- Confronting and preparing for death (From Block 2001, p. 2900)

How can we help patients achieve these goals? Dr. Ned Cassem, a talented psychiatrist and teacher who worked extensively with dying patients, articulates nine components essential to care of the dying (Cassem 1991):

Components of Care of the Dying

- Clinical competence
- Comfort
- Compassion
- Consistency and perseverance
- Cheerfulness
- Equanimity
- Visits from children
- Family cohesion and integration
- Communication

Of these components, the keys for me have been acquiring the clinical competence to ameliorate a patient's physical and psychological distress, the communication skills to help them as they struggle with questions about their goals of care, and the equanimity to remain present with them. When a patient is lucky enough to experience increased physical, psychological, and spiritual comfort, it becomes much easier for his family to be near and, if they wish, to be present at the time of death.

Caring for a Dying Physician

There are special challenges when our patients are themselves physicians. Fromme and Billings described these well in their 2003 article: "Care of the Dying Doctor: On the Other End of the Stethoscope." They report that physicians have a greater anxiety about death than do members of the general population, and although physicians may understand more about what is happening to them, they have no more emotional resources to deal with their dying than other people do. The oncologist who is caring for a physician may feel an extra sense of obligation, along with a heightened sense of vulnerability, since this is happening to "one of us." Fromme and Billings caution us not to succumb to "VIP" syndrome, where we give the patient too much control, and we lose our usual boundaries; this often results in patients getting worse care from us. We can help by being aware of and compassionate about physicians' attempts to self-doctor and to retain control and self-respect, and by trying to maintain our equanimity. At the same time, we need to remain open to a connection with our physician patients, allowing them the same space to grieve and to share their distress, hopes, values, and goals as we do with any other patient. Fromme and Billings end by offering several strategies, including a detailed table describing how to negotiate the relationship and helpful insights into how the physician patient is both "like all patients" and "different."

Supporting the Family

The dying patient presents an increased burden for an already stressed family, especially when the patient is dying at home. But families who have been able to care for a dying loved one at home often express their profound satisfaction that they did everything they could. Even those who need to bring the patient to the hospital for the final few days or hours may feel an appropriate sense of pride and accomplishment.

Most family members have never seen anyone die, and although willing to do whatever is necessary to allow the patient to die at home, they are totally unprepared for the reality of that death. When I was still practicing oncology, as a patient entered her final weeks to months, I met with or talked on the phone with the patient and her family whenever possible to review the implications of allowing the patient to die at home. Along with the nurses and social workers on my team, I found I needed to validate caregivers' requests for additional home care resources or, if the patient and caregiver preferred, to move the patient to an inpatient hospice or nursing facility in which she could receive hospice services. Enrolling patients in hospice is one of the most important things you can do to enhance the bereavement of those they will leave behind; their bereaved survivors will be less likely to develop a major depressive disorder, prolonged grief disorder (see below), or post-traumatic stress disorder. They will even be less likely to die themselves (Christakis and Iwashyna 2003; Bradley et al. 2004; Wright et al. 2010).

PRACTICE POINTS: COMMUNICATION DURING THE LAST DAYS

- Have a family meeting to discuss what is likely to happen next.
- Call frequently to give support and to adjust the medical regimen.
- Mention that patients often need family permission to let go and reassurance that the survivors will be OK.
- Tell the family Dr. Byock's "Five Things" (Byock 1997): I forgive you; forgive me; I love you; thank you; and good-bye.
- Provide written reminders: "Don't call 911"; "Signs and symptoms of dying"; "Who to call for help"; "What to do when death occurs."
- Assuage ethical or religious concerns about symptom management.
- Revisit the benefits of hospice care.

If a hospice program does not fit the family's needs, a "bridge to hospice" program can help them provide care at home by arranging for home care nurses and health aides and for delivery of hospital beds, commodes, and oxygen if needed. Caregivers are particularly prone to becoming exhausted and frustrated if they are trying to provide this care alone, and we must validate their need for help.

When the patient was likely to die in a matter of weeks, I talked with caregivers about how their roles in the care of their loved one now needed to change. Before, they were the eyes and ears of the oncology team, monitoring the patient

for early warning signs as he rode the roller coaster typical of chemotherapy treatments. Families may not even realize that this monitoring of blood counts and being hypervigilant for any signs of deterioration have become second nature to them. They need to know that they can now relinquish those tasks without exposing the patient to danger, and that they have equally important tasks to work on in the time that remains. Patients have stories to tell, meaning to make, legacies to leave—and likely need help with these and with maintaining a sense of purpose. We also encouraged patients and their families to work with hospice programs to aid them in these tasks. Communication, in fact, was key to our support of the patient's family members throughout their ordeal.

When a patient who was not enrolled in a hospice program was dying at home, I made every effort to call the patient and the family two or three times a week, increasing the frequency for the last few weeks. I think that the calls were particularly helpful for the caregivers. I answered their questions, provided emotional support, praised their efforts, and demonstrated my continuing concern. I also had the opportunity to modify the patient's treatment regimen frequently to ensure the best possible control of symptoms during those last days.

PRACTICE POINTS: THE TRANSITIONAL PHASE

- Increased somnolence
- Loss of appetite
- Weakness
- Confusion
- Falls
- Incontinence

(From Doyle-Brown 2000)

Family members often want to know how they will recognize that the last days are approaching. Some want to know how to focus their care. Over the course of the patient's illness, after all, they have frequently needed to be enthusiastic coaches; without their urging, the patient would not have bounced back as readily from what proved to be temporary setbacks. But if the patient is dying this time, it is important to let family know, so that their goals as caregivers can change. For some who would like to be at home with the patient, vacation, sick, and even family leave days are limited, as is the time for which another person can assume that person's other obligations. Caregivers need to know when to

take that time or to call in extra help, so that they can feel free to be present full time with the patient during the important last few weeks.

What are the signs of what Doyle-Brown (2000) has termed "the transitional phase" (i.e., before the patient becomes bed-bound), and what effects do they have on the family? Characteristics that denote the beginning of this phase include increased sleep, almost total loss of appetite, and then weakness. Some caregivers mistakenly believe that the patient has some control over this phase, and they may be angry at the patient, thinking, "He's giving up!" As I discussed in Chapter 4, repeated rejection of specially prepared food is particularly distressing. Confused patients fight to remain as independent as they think they can still be, and some are not fully convinced that they need help, until they have fallen or become incontinent.

When it seems appropriate, remind the caregivers that it is important to give the patient "permission" to die. I learned this many years ago from one of my residents. One day on rounds, John gently told me that a patient of mine, Mr. Garabaldi, was "holding on" because he didn't want to let me down—that I was the only one Mr. Garabaldi hadn't told that he wanted to die. I felt chastened and went to visit Mr. Garabaldi that afternoon. During our visit, I reassured him that he would not be disappointing me, that I knew he had been fighting for a long time, and that I understood his need to rest. His relief was obvious, and he died within the week.

Up until that point, I had no idea how important it was to tell someone explicitly that he can "let go." It does not matter whether the patient can respond verbally or indicate in any way that he has heard you; it still needs to be said. Share this insight with family members and urge them to give this kind of permission to their loved one. And ask them to tell the dying person not to worry about them, that they will be OK.

Dr. Ira Byock, in *Dying Well,* lists an additional "Five Things" that both the dying patient and the family members need to hear: I forgive you; forgive me; thank you, I love you; good-bye. Some families say these things more easily than others, but almost all will eventually be able to say one or more. When they do, both family members and patients seem much more at peace.

Written reminders. If the patient is enrolled in a hospice program, the hospice nurses or social workers give the families written reminders of how to reach them. They suggest that the family put these somewhere they will easily find them in an emergency, such as on the refrigerator or stuck onto a coffee maker. Someone from the hospice program can be reached 24 hours a day, 7 days a week.

Some states have out-of-hospital DNR forms or the MOLST or POLST forms that I described in Chapter 4. These should also be put in a prominent place, like

on the refrigerator. In addition, encourage someone in the family to inform the local ambulance company that the patient has an advance directive and does not want to be resuscitated. You can even send the ambulance company a copy of the directive to keep in its files. Then, if 911 is called by mistake when the patient dies, the paramedics will know not to institute cardiopulmonary resuscitation.

It's also helpful to reiterate in the written reminders how to reach you or your covering physicians in an emergency. If the patient is not followed in a hospice program, ask the family members to call you when the patient dies and to tell the funeral director that you will be responsible for completing the death certificate.

The family's ethical concerns about pain management. Despite many reassurances to the contrary, a major source of concern for family members is giving pain medicine to someone who is dying. They fear that in trying to relieve pain, they might inadvertently be hastening death. Even though they cannot relieve the person's suffering in any other way, they may have religious concerns—often because they are not aware of the writings of their religious leaders on this subject.

I discussed in Chapter 2, and it is worth reiterating here, that Catholicism, Orthodox Judaism, and Islam all encourage the relief of suffering, even if there is a chance that, as a secondary effect, the person may die sooner than if the pain medicine were withheld. This is the so-called doctrine of double effect (Bradley 2009). The Catechism is very clear on this point: intent is the key. Unlike Roman Catholicism, Islam and Orthodox Judaism do not have one spokesperson, but in recent writings, the majority of opinions from clerics of both faiths are identical to that of the Roman Catholic hierarchy: if the intent of the caregiver or the physician is to relieve the patient's pain, the caregiver should give whatever medication is required. These three religions are also in concert about the right of the patient to refuse artificial means of prolonging life (e.g., respirators, dialysis, high-flow oxygen, CPAP) or other therapies that delay a natural death. Artificial nutrition or hydration can also be withheld if they are only prolonging the dying process. But Roman Catholic patients have been advised, "There are many living wills and advance directives that invite patients to remove food and water provided by artificial means should they become incapacitated. Catholics should not sign such documents . . . A better alternative is the designation of a health care agent, who can, case by case, make a determination of the morality of medical interventions consistent with the will of the patient and the teaching of the Church" (Bradley 2009, p. 376).

Referral to a hospice program. Even if the patient or the family has previously resisted accepting the referral, make every effort to engage hospice services for dying patients, including those dying in hospitals or in long-term care facilities. Hospice program eligibility and a full description of the services provided

and of the ongoing role for the oncology team are given in Chapter 4. The hospice clinicians may have useful suggestions for improving the patient's symptoms and will also address psychological, social, and spiritual sources of distress of the patient and family. Hospice personnel begin to prepare the family for their loss and offer continued assistance through bereavement programs that continue for more than a year after the death.

In a period as short as the few days or week before death, hospice care can be an enormous source of comfort to families and professional caregivers, particularly when they have never witnessed a "natural" death. The team members have "been there," can explain what is likely to happen, and can provide expert symptom management during the last hours or days. For patients at home, hospice staff will provide practical instruction in how the family can help with toileting, feeding, massage, and giving medications. As the patient's death approaches, hospice personnel provide suggestions for answering the patient's questions and written materials that explain how the family or the staff in the inpatient or long-term care facility can determine that death is imminent.

When Patients Die in the Hospital

Discontinuing the Devices

Oxygen. Oxygen delivered by nasal cannula or mask, or by noninvasive ventilation (including high-flow oxygen, continuous positive airway pressure [CPAP], and biphasic positive airway pressure [BiPAP]) is often used for patients with respiratory insufficiency. Oxygen can enhance day-to-day function, and noninvasive ventilation can support patients through pneumonias, cardiac decompensations, or side effects of antineoplastic therapy, preventing the need for intubation. As the end of life approaches, oxygen is often continued for these patients and for patients with extensive pulmonary metastases who want to interact with their loved ones, and be as alert and active as possible.

The challenges arise when patients on such support are within days of death. Although patients and their family members usually are willing to continue to accept nasal oxygen or oxygen delivered by a mask, they often want to discontinue the uncomfortable noninvasive ventilation (i.e., high-flow oxygen, CPAP, or BiPAP) when they are sedated by the medications they need for comfort and they are no longer able to interact. They ask us to discontinue the technology that they consider to be prolonging their dying.

Patients of course have as much right to have these discontinued as they would to have an endotracheal tube removed. Noninvasive ventilation is a tech-

nology that can prolong someone's dying. It can be easier to "see" that CPAP and BiPAP are uncomfortable and understand that someone would want them removed. The high-flow oxygen (at 35–50L/min of 100% oxygen) can appear innocuous, and clinicians may ask themselves, or each other, why that should be stopped, when the patient is going to die even if it is continued.

In fact, that was what I was asked by the nurses and house staff caring for one of the patients we saw on the inpatient palliative care consultation service.

Vera was a 49-year-old woman from Vermont who had extensive metastatic bronchoalveolar cancer that was refractory to therapy. She was of the Catholic faith and was married to Evelyn; they had been together for 25 years and had three children, 20, 18, and 15 years old. Vera and Evelyn told us that over the last weeks, they had hoped that her breathing would improve. Now they understood that this was not possible, and that the medications we needed to use to make Vera more comfortable would also sedate her. They knew that soon, she would not be able to be both awake and comfortable.

When that time came, when Vera had to be sedated continuously, they asked that her dying not be prolonged, that the continuous high-flow nasal cannula delivering 40L/minute of 100 percent oxygen be discontinued, that she be allowed to die, and that she be medicated additionally if needed for comfort. They did not want her death "artificially prolonged by machines," as they put it.

As you can imagine, considerable discussion ensued among the inpatient team, the outpatient oncology team, the palliative care team, and the ward staff. We asked that an ethics consult be called, to help us, her professional caregivers, think about what our rights and obligations were to Vera, and what our ethical response to the request could be. We invited Father Hal, the Catholic chaplain who had been visiting Vera regularly, to participate in the discussions.

First, we reviewed the facts of the case with Philip, our ethics consultant. The physicians agreed that no specific therapy could reverse her pulmonary process or make Vera more comfortable. We and Philip also agreed that Vera had the mental capacity required to make this request. To be considered to have capacity, a patient must be able to "1. Make and communicate choices; 2. Understand relevant information; 3. Appreciate the clinical situation and its consequences; 4. Manipulate information rationally; and 5. Make a decision that is consistent with the patient's values and goals" (Lampert et al., p. 1010). Vera was able to do all of these; she understood that the implications of her request were that she was likely to die within minutes to an hour of it being carried out. Her outpatient oncology team told us that the request was consistent with Vera's long-held and expressed values that when the time came, she did not want her death to be prolonged.

Philip then asked the staff what questions they had or feelings they wanted to share. Many said they "knew" that discontinuing unwanted high-flow nasal oxygen was the same as discontinuing an unwanted endotracheal tube, but that it felt very different to them. They wondered why we couldn't just keep Vera asleep and comfortable for the days or week it would likely take her to die despite the supplemental oxygen.

Philip shared that these were the kinds of conversations he used to have fifteen years ago in the ICU after the Supreme Court first ruled that patients had the right to refuse artificial technological prolongation of their lives, and patients like Vera were first extubated at their request. That "felt wrong" too, initially, but now it is accepted practice. Philip reminded us that extubating someone or removing high-flow oxygen were medically and ethically the same, and Vera had the right to refuse both. What would be wrong would be to deny her this right.

Some of the younger graduate nurses asked whether this was euthanasia, or physician-assisted suicide. Philip replied that since Vera would die of her underlying disease within minutes to hours of the ventilation being stopped, hers was not a request for euthanasia or assisted suicide. Stopping the oxygen was not euthanasia because our *intent* was not to kill her, but to allow her to die of her disease. And it was not physician-assisted suicide (more properly termed physician-assisted death) because that involved giving a patient a prescription for a fatal dose of medication that she would take herself (I review the distinctions in more detail in Chapter 4).

One of the inpatient physicians asked Father Hal whether he felt Vera would be committing suicide. He replied that, on the contrary, she was choosing not to have her natural death prolonged by machines. He quoted for us the portion of the Catechism of the Catholic Church that confirms that patients are not required to acquiesce to having their lives prolonged by any means possible, and that in allowing themselves to die naturally, they are not committing a sin. "Discontinuing medical procedures that are burdensome, dangerous, extraordinary, or disproportionate to the expected outcome can be legitimate; it is the refusal of 'overzealous' treatment. Here one does not will to cause death; one's inability to impede it is merely accepted" (*Catechism of the Catholic Church* 1997, Subheading I, Respect for Human Life, verses 2278, 2279).

After more discussion, her nurses and her medical teams felt they understood her request and their ethical obligation to her. When the time came to honor Vera's wish, we were able to remove the high-flow cannula and, using the same sedatives and opioids we would use if we were physically extubating her, keep her asleep until she died, less than half an hour after the oxygen was stopped.

The process we engaged in—transparent discussion of the request and its implications with all the caregivers, with the guidance of an ethics consultant

and the participation of chaplaincy—is one that we have used whenever we need to perform a similar "extubation" in a non-ICU setting in the hospital. A week or two afterward, we offer to return to the unit to "debrief" with any staff who have remaining questions or feelings to share.

Cardiovascular implantable electronic devices (CIEDs). Similar ethical challenges arise for caregivers of patients who have had implanted cardioverter defibrillators (ICDs), implanted pacemakers (PMs), or cardiac resynchronization therapy (CRTs). In 2010, a position paper was published on patients nearing the end of life or who were requesting that the therapy be discontinued; it had been created and was endorsed by the American College of Cardiology, the American Geriatrics Society, the American Academy of Hospice and Palliative Medicine, the American Heart Association, the European Heart Rhythm Association, and the Hospice and Palliative Nurses Association. Among its authors was George Annas, a noted bioethicist.

The authors included a thorough review of the basic principles of decision-making. And they made the point that in all the cases before the Supreme Court, the right of the patient to refuse a life-prolonging measure was upheld. They concluded that since the Court never distinguished among life-sustaining treatments, the rights apply to CIEDs even though these are not expressly mentioned in the decisions, because they all are life-sustaining therapies. Even pacemakers do not reverse the underlying terminal cardiac condition and so can be discontinued if the patient chooses.

In my experience, however, most clinicians feel that pacemakers are not harmful and will not prolong life once the patient's heart can no longer respond to them. They may agree to disable the portion that responds to the tachyarrhythmia but have difficulty disabling the part that responds to the bradyarrhythmia. In fact, as many as 10 percent of physicians caring for these patients consider discontinuing a pacemaker a form of assisted suicide or euthanasia (Lampert et al. 2010). I have experienced resistance to discontinuing a pacemaker in a patient whose bradycardia would be fatal if the pacer were inactivated. In such a situation, if the patient has the capacity to make the request (as I discussed earlier), and the physician is unable to carry it out for moral, religious, or ethical reasons, it is incumbent upon him to transfer the care to another physician who can (Lampert et al. 2010).

Cardiologists are more willing to turn off the implanted defibrillators, however, after comfort-focused care is begun. Otherwise, 20 percent of patients in the last weeks of life receive painful shocks (Lampert et al. 2010). Reprogramming or a magnet is needed, and since this is more difficult to arrange for outpatients, it is done whenever possible while the patient is still an inpatient.

As for the decision to discontinue any CIED, I recommend that you engage in a process similar to the one I described for discontinuing ventilatory support. Having a procedure in place or a hospital guideline that includes involvement of palliative care teams, chaplains, and ethics consultants will help support the teams who need to make these difficult decisions and then carry them out. The position paper by Lampert and colleagues provides very useful guidance in this regard (Lampert et al. 2010).

Supporting the Inpatient Ward Team

When one of the patients we are following is dying in the hospital, we feel the additional obligation of helping the primary oncology team, the house staff, and the ward staff (social workers, nurses, patient aides, the environmental services staff, and ward clerks) cope not only with the patient's and family's needs but with their own feelings of distress. The dying process often brings ward staff closer to patients and their families, even if this is the patient's first admission to that ward.

To allay feelings of guilt and anxiety, we review with all team members the history of the illness, the limits of the treatments that remain, the burdens of those treatments, and, when appropriate, the limits the patient has placed on further supportive measures. We also remind them that, despite our best efforts, patients still die and that it is no one's fault. This can be very comforting. Even more helpful is suggesting things they can do that will enhance the patient's last days and further the healing process of the survivors.

PRACTICE POINTS: SUPPORTING THE INPATIENT WARD TEAM

- Remind the team of medicine's limitations in the face of illness that is refractory to treatment.
- Relieve anxiety and unwarranted guilt; explain patient and family anger.
- Develop a plan of care through which they will minimize patient and family suffering.
- Dispel misconceptions and praise their efforts.
- Record and update advance directives regarding elective intubation and resuscitation.
- To enable a truly informed choice, give realistic prognoses and realistic descriptions of the burdens and benefits of remaining therapeutic options, including mechanical ventilation.

Not uncommonly, however, house staff are the undeserving target of a patient's or a family's anger, as was the case for Mr. Champion's team.

Mr. Champion

Mr. Champion underwent definitive therapy for lung cancer, but six months later, he was admitted for bilateral malignant pleural effusions. He required bilateral chest tubes and sclerosis, was febrile from resistant pneumonia, and was significantly malnourished. Despite control of his pain, Mr. Champion was unable to clear his numerous secretions, was severely tachypneic, and became recurrently hypoxic. No pulmonary emboli or clots were present in his upper or lower extremities.

Although Mr. Champion had told his oncologist, Dr. Rydell, that he did not wish to be intubated electively or resuscitated if that meant he would have to be on a respirator, no advance directive was on his chart. Because of Mr. Champion's rapidly deteriorating pulmonary status, I asked Dr. Rydell to confirm and document that Mr. Champion did not wish to be electively intubated.

The next morning, nurses on the unit told me of the conversation they had overheard between a furious Mrs. Champion and the house staff. It went something like, *"Why did you have to ask Dr. Rydell to talk about those things with my husband? Look what you've done to him. You took away all his hope! He was fine until you made us have that talk—now look at him!"* She went on in this vein for some time, and the next day she would not speak with the physicians whom she blamed for her husband's ongoing deterioration.

After Dr. Rydell confirmed that Mr. Champion did not wish to be intubated, the team treated his progressive dyspnea symptomatically with pulmonary toilet, suctioning, oxygen, antibiotics, anxiolytics, and opioids. He died two days later, apparently comfortably. As we gathered around him, his wife asked the house staff's forgiveness *"for what I said out there in the hall."* She included the doctors in the prayers she led, and in the thank-you gift she sent to all the floor staff later in the week.

Not all house staff teams are so lucky. Mr. Champion's wife was able to understand that in her grief, her anger had been misplaced and to apologize to the staff. Many families don't, and the interns, residents, students, and nurses caring for the patient add the family's unjust accusations to their own unwarranted feelings of guilt about the patient's death.

Be sure to support the house staff through these stressful situations. Explain that they are often the lightning rod for the family's or patient's helplessness, despair, grief, and anger. Encourage them not to take family attacks personally, to continue their exertions on the patient's behalf, and to work with the palliative care team to eliminate or minimize sources of distress. During hospitalizations

that lead to death, and after the death itself, dispel any misconceptions the staff may have about their "fault" for the death and praise the work they did to make the dying person as comfortable as possible. Praise coming from nurses who have shared in the care of the patient can be particularly healing. In turn, you can encourage the house staff to praise the nurses for the care they have delivered. This kind of support goes a long way toward enabling young physicians and ward staff to recover from the pain they experience when a patient dies and to allow themselves a feeling of satisfaction for a job well done.

Resuscitation status. In Mr. Champion's case, as the crisis neared, Dr. Rydell simply needed to confirm that Mr. Champion's wishes had not changed. Later, when intubation would have been needed to support him (his pH was 7.24, pCO_2 80 mm Hg, and pO_2 55 mm Hg on a 100 percent rebreathing mask), we all felt confident that in not intubating him, we were caring for Mr. Champion within the limits he had set.

Unfortunately, the 1995 SUPPORT study (of patients dying in teaching hospitals) indicated that physicians often do not know the wishes of their hospitalized patients suffering from life-threatening illnesses—only 47 percent were aware that their patients did not wish to be resuscitated. One-third of outpatients had not even told their physicians that they had an advance directive.

We still have a long way to go in this area. A 2011 review concluded, "The persistent problems with DNR suggest that physician behaviors toward communication with patients about goals of care and resuscitation decisions have not measurably changed in the past 20 years" (Yuen et al. 2011, p. 795). They cite one study, for example, of 500 patients who had a cardiac arrest during a hospitalization. When these patients were admitted, 89 percent would have been able to participate in a DNR discussion, but by the time the DNR discussion actually occurred, only 24 percent were able to do so.

We should do all we can to inform ourselves of the wishes of patients with far-advanced disease while they are still well enough to make rational decisions, and we should communicate these directives to all members of their health care teams in and out of the hospital. As hard as it may be, it is a gift to your patients with nearly refractory cancer to be realistic when you inform them of the extent of their disease, the likelihood that the remaining treatments will add meaningfully to the time they have left, the realities of mechanical ventilation, and the odds of ever being weaned from it; you will empower them to make informed decisions about resuscitation and preventive intubation and you will avoid the need to introduce these difficult topics first in crisis situations. I predict that if you have these conversations earlier, patients whose disease is essentially untreatable

and who might be able to die comfortably will be resuscitated much less often, saving both them and their families needless suffering.

Supporting the Families of Inpatients

Despite our best efforts to enable those who wish to die at home to do so, many patients who have cancer require such complex care that they must remain in the hospital until they die. Our palliative care team is often consulted to help care for these patients and their families. The families may have promised to take the patient home and are feeling distraught at what they see as their failure to fulfill the patient's last wish.

I recently cared for Elmo, a 45-year-old man who required significant respiratory support, more than could be delivered in any other setting. Some hospitals have one or two rooms they have redecorated as "comfort suites" for these patients; they look something like a very nice hotel room, or home, with ample space for friends and family to stay overnight, but they also include the technology and nursing care the patients need to remain comfortable as they die.

Our hospital does not have rooms like these, but we were able to do a number of things to assuage Elmo's family's feeling that they had let him down, and to support them. We were clear that it was a medical decision that was keeping him in the hospital, not any concern we had about their love for him. We said that while we, too, had wished we could ensure his comfort at home, we just could not; we needed to care for him in the hospital.

Then we asked them to make Elmo's hospital room look, sound, and smell like his room at home and encouraged them to bring bed covers, pictures, one of his son's favorite stuffed animals, music, whatever would make it feel more familiar. We allowed them unlimited visiting hours and provided drinks and snacks so that they would not have to leave the floor.

Elmo was unstable enough that we successfully enrolled him in a hospice program at the inpatient level of care, and the hospice team came daily to provide him and his family extra support, which they appreciated. When Elmo died, he was completely surrounded by his family members. We let them know that the last faces he saw, the last voices he heard, the last touch he felt was that of his family, and that they had done everything any family could do to help him have his wish: home, after all, is the place where you are with those whom you love and who love you, and they created that in the hospital, for him. It is my hope that as they told the story of Elmo's death, pride at what they had been able to do for him would replace any regret that he had to die in the hospital.

Symptom Management Guide

Symptom management in patients' last days can be challenging. The SUPPORT study also revealed that family members often felt the patient's symptoms were not adequately controlled. Researchers found that among the conscious patients, family members thought that 40 percent had unrelieved severe pain and, of those with lung cancer or an underlying malignant condition with superimposed multisystem organ failure, that 70 percent had severe dyspnea and 25 percent had moderate anxiety or dysphoria (Lynn et al. 1997).

Symptoms change rapidly during these last days. If possible, when the patient is dying in the hospital, be present for at least five to ten minutes several times a day. Sit at the bedside and observe the patient for any signs of pain, delirium, excessive upper airway secretions ("death rattle"), or myoclonus. If you find them, correct them as suggested in the following pages. Ask family or friends who are there what they have observed, and answer their questions. Let them know they can touch and speak to the patient, as they may be afraid to do so if the patient is attached to a number of machines or intravenous lines.

You can also help ensure that the patient's spiritual needs are met. Inquire if Catholic patients wish to receive the Sacrament of the Sick (formerly referred to as "Last Rites"), which must be given while the patient is still alive. Even patients who have refused visits from a chaplain or a priest may want to receive this sacrament. Also inquire of members of other faiths if there is anything you need to know to care for the dying patient in a way that is consonant with their religion. Let them know the family's spiritual advisors are welcome to visit at any time, and that you and your team will do all you can to accommodate the patient's spiritual or religious needs (such as placing Muslim patients facing the East).

Symptom Complex of Dying Patients

Data on the frequency of the various symptoms that occur in the last days to week before death are somewhat conflicting. Patients usually have multiple symptoms, with combinations of those listed below varying with the underlying disease process:

- Pain
- Noisy or moist breathing
- Urinary incontinence or retention
- Restlessness, agitation

- Dyspnea, cough
- Nausea and vomiting, anorexia, dysphagia, xerostomia
- Delirium
- Fatigue
- Existential or spiritual distress
- Cooling of extremities
- Fecal incontinence

Up to 70 percent of patients with advanced cancer have pain, and this pain requires ongoing therapy until death. Noisy or moist breathing, urinary incontinence or retention, and restlessness and agitation are seen in almost half of patients who are actively dying.

MANIFESTATIONS OF ACTIVE DYING: THE LAST 10 TO 14 DAYS

- Dehydration, tachycardia, followed by decrease in heart rate and blood pressure
- Perspiration, clammy skin, cool extremities; just before death, mottling
- Diminished breath sounds, irregular breathing pattern with periods of apnea or full Cheyne-Stokes respiration; grunt or moan with exhale
- Mouth droop; difficulty swallowing; loss of gag reflex with pooling of secretions, causing "death rattle"
- Incontinence of bladder or rectum
- Agitation ± hallucinations; stillness; patient is difficult to arouse

(From Pitorak 2003)

One in five patients will be short of breath, and about one in ten will have nausea and vomiting. The incidence of delirium in patients dying of advanced cancer is 88 percent (Lawlor et al. 2000). Manifestations of delirium include sweating, confusion, jerking, twitching, or plucking at bed sheets.

Patients lose the ability to swallow and become much less interactive. It is as though they are living in a large mansion in which they gradually move to rooms that are farther and farther from the front door. Responding to voice or touch takes them much longer, and they may stop showing any response. Most families seem to understand that the patient is not personally rejecting them and are happy to let patients know that they need not respond. I often say that it just takes too much energy for the patient to "come to the front door" to the friends and family that are constantly around, but let them know that the patient might

open his eyes or otherwise respond when a new person comes or there is a new voice on the phone.

Some patients may experience existential or spiritual distress, but others articulate visions of spiritual peace. One night at midnight, an Indian patient I cared for asked her husband for "water from the Ganges." Until then, he had seemed not to understand how ill she was. But after the request, he realized she was dying. They were able to grieve together, talk, and say their last good-byes. She died the next morning. And an Irish patient spoke glowingly to me of "going to the Isle to meet my people." She could see them waving at her. Could I? Her eyes were closed as she added, "My job is to get there. They're waiting for me." She continued to speak, but in Gaelic. As I got ready to leave, I wished her a peaceful journey. To my surprise, without opening her eyes, she said, in English, "Thank you."

Commonly Required Medications

Most of the problems experienced by dying patients can be controlled by a limited number of medications given by the rectal, transdermal, or, if necessary, parenteral route (Table 10.1) (McPherson et al. 2012). Medications are usually needed for pain, for rattling secretions, and for terminal anxiety, agitation, or delirium. Some patients need treatment for dyspnea or various other miscellaneous problems.

Although it would be wonderful if patients who were no longer able to take oral medications could absorb medications through their intact skin in gel form, *this does not work*. Compounding pharmacies commonly make gels with antiemetics or anti-anxiety agents in them, but there is no evidence that these are absorbed through intact skin (Smith et al. 2012). Haloperidol, diphenhydramine, metoclopramide, and lorazepam can be absorbed through the rectal mucosa, as I will describe below, but they are not absorbed from intact skin, and recurrence of symptoms may follow a change to a gel format.

Liquid concentrates, subcutaneous infusions, and, rarely, intravenous infusions will ensure symptomatic relief for most patients. For those few patients whose distress cannot be controlled any other way, it may be necessary to consider palliative sedation to unconsciousness (see below).

Pain control. If one uses the WHO guidelines for cancer pain relief (see Chapter 6), 50 percent of cancer patients near death will have no pain, 25 percent mild to moderate pain, and only 3 percent severe pain. Patients require close monitoring, and both opioids and nonopioid adjuvants are usually required.

If the patient is unable to take pills, transmucosal, sublingual, rectal, or transdermal opioids are usually effective. In some cases, however, subcutaneous

Table 10.1 Treatment of Common Problems in the Final Days

Problem	*Agent*	*Route; Dose*
Baseline pain	Concentrated oxycodone or morphine solution	p.o.; SQ q4h around the clock; individualized
	Fentanyl	Transdermal; individualized
	Methadone liquid	p.o.; individualized
	IR Morphine / hydromorphone suppositories	p.r. q4h
	SR opioids put in gel capsules into the rectal vault	p.r. q8 to 24 hr depending on the preparation's usual oral schedule
	NSAIDs: acetaminophen, naproxen	p.r. t.i.d. to q.i.d.
	Dexamethasone (requires compounding)	p.r. daily to b.i.d.
Breakthrough pain	Concentrated oxycodone or morphine solution	Sublingual, SQ q4h; individualized
	Fentanyl	Transmucosal[1] (buccal, sublingual); individualized
Death rattle	Scopolamine	Transderm Scōp, 1–3 patches q3d; 0.1–2.4 mg / 24 hr SQ, IV
	Hyoscyamine (Levsin SL)	0.125–0.25 mg sublingual q4h (discontinue when renal function declines significantly)
	Glycopyrrolate (Robinul)	0.2–0.4 mg SQ, IV t.i.d. to q.i.d. or 1–2 mg p.o. b.i.d. to t.i.d.
	Atropine	0.4 mg sublingual, SQ, IV q4–6h
	Atropine 1% opth solution	1–2 gtt sublingual, p.o. q4h
Anxiety	Lorazepam (Ativan)	1 mg p.o. or sublingual q2h
	Diazepam suppository	5 to 10 mg p.r. daily
Delirium	Haloperidol (Haldol)	2–4 mg p.o., SQ, IV q30min p.r.n. to total 20 mg / 24 hr
	Olanzapine (Zyprexa, Zydis)	2.5–5 mg p.o. / sublingual qhs to b.i.d. plus p.r.n. q4h
	Chlorpromazine (Thorazine)	25–50 mg p.o. q4–8h or 25 mg p.r. q4–12h; preferred for dyspnea
Dyspnea due to anxiety/panic	Lorazepam (Ativan)	1 mg p.o. or sublingual q2h
	Morphine	5–10 mg sublingual, IV, or by nebulizer
	Chlorpromazine (Thorazine)	25 mg p.o., p.r. q4–12h; or 12.5 mg IV q4–8h

Note: Medications compounded into gels are NOT absorbed through intact skin (Smith 2012). All liquid p.o. medications can be given per g-tube.

[1]Only for opioid-tolerant patients.

or, when intravenous access is available, intravenous infusions will be needed. Concentrated morphine or oxycodone solutions (20 to 40 mg/ml) can be given hourly or every 2 hours and are often satisfactory. Rectal administration of sustained-release opioid preparations is not approved by the FDA, but studies indicate that morphine absorption from a sustained-release preparation placed in the rectal vault is equivalent to that from oral administration, and oxycodone levels will be greater than those achieved when the patient takes the pills by mouth. If pain is a new problem, and the patient is opioid-naive, institute therapy with 15 to 30 mg of sustained-release morphine rectally every 12 hours. Alternatively, in patients with adequate fat reserves, place a fentanyl patch and administer a liquid or rectal opioid for the first 12 hours until the blood level of fentanyl is adequate for pain relief.

As many as 50 percent of dying patients need an increase in opioid dose during their last days. If the calculated opioid dose is too large to be delivered by sublingual, transdermal, or rectal routes; if pain relief does not seem to be satisfactory using any of these routes; or if the routes are unacceptable to the patient or the caregiver, give the opioid by subcutaneous infusion or, if intravenous access is available, by intravenous infusion. Both types of infusion can be delivered in the home with the aid of hospice or other home nurses. The starting opioid dose for a patient whose pain is well controlled should be the intravenous equivalent of the oral dose (see Table 6.5); if the pain is not under control, give a dose that is slightly higher than the equivalent dose.

Adjuvants should also be continued. When the patient is no longer able to take oral medications, they can be given rectally (Samala and Davis 2012) or subcutaneously. Patients previously benefiting from oral NSAIDs can receive rectal

PRACTICE POINTS: MEDICATION FOR PAIN CONTROL WHEN PILLS CANNOT BE SWALLOWED

- Concentrated IR morphine/oxycodone (20 to 40 mg/ml), buccal or sublingual.
- Sustained-release preparations, p.r.; methadone liquid, buccal or sublingual or in feeding tube if one is already in place; consider converting to an opioid infusion SQ or IV.
- Adjuvants, p.r. (e.g., NSAIDs, acetaminophen, doxepin, dexamethasone).
- Do not start an opioid continuous infusion (e.g., a "morphine drip") if the patient has not required opioids before and is not in sustained pain.

aspirin, naproxen, ibuprofen, or diclofenac, and suppositories of indomethacin and acetaminophen are commercially available; patients taking a stable glucocorticoid dose for bone or nerve pain can receive subcutaneous dexamethasone or specially compounded dexamethasone suppositories. Rectal doxepin can replace oral tricyclic antidepressants.

Death rattle. Patients are usually unaware of these loud respirations, but they can be very distressing for families. They occur in 60 to 90 percent of dying patients. Sometimes, simply repositioning the patient is helpful because he may breathe more easily in a lateral recumbent position than supine. Most patients benefit from one of the drying agents, such as oral hyoscyamine (Levsin SL); scopolamine in a transdermal patch; intravenous or oral glycopyrrolate; or intravenous or oral atropine (via 1 percent ophthalmic drops). To minimize toxicity when renal function worsens, discontinue hyoscyamine if possible and reduce doses of glycopyrrolate.

PRACTICE POINTS: TREATMENT OF DEATH RATTLE

- Place the patient in the lateral recumbent position.
- Administer drying agents:
  - —Hyoscyamine (Levsin SL), 0.125–0.25 mg sublingual q4h (except in patients with renal failure).
  - —Scopolamine
    Transderm Scōp, 1 to 3 patches every 3 days.
  - —Glycopyrrolate, 0.2 to 0.4 mg IV t.i.d. to q.i.d. or 1 to 2 mg p.o. b.i.d. to t.i.d.
  - —Atropine, 0.4 mg sublingual, SQ, IV q4–6h; 1–2 gtt 1% ophthalmic solution p.o. q4h.

None of these anticholinergic agents has been shown to be better than the others in controlling secretions of dying patients. Scopolamine and atropine, however, cross the blood-brain barrier, so I use glycopyrrolate or hyoscyamine if I am worried about increasing the patient's confusion or causing or exacerbating delirium. I also take into account the routes that are available and what the patient prefers. If you prescribe one of these agents, the patient will also need to have his mouth moistened periodically.

Terminal restlessness. Almost half of patients who are actively dying of cancer show signs of restlessness and agitation. They may toss and turn, moan, have

muscle twitching or spasm, and only intermittently be awake. Even though patients may appear to be out of contact with the external world, they often seem to be reassured by familiar voices or by being touched.

The agitation is sometimes due to reversible physical problems, such as a full bladder, fecal impaction, pain, nausea, or trouble breathing due to hypoxia or poorly cleared secretions. In other patients, unresolved spiritual, psychological, or social problems induce the distress. All members of the hospice team will reevaluate the patient with these issues in mind. They can often detect the cause of the problem and offer workable solutions.

Patients may need a mild sedative such as lorazepam (e.g., Ativan) or diazepam (e.g., Valium) suppositories if they are unable to take oral medications, spiritual reassurance, a visit from an estranged family member or friend, or just permission to "let go." When it is possible to arrange these, the anxiety often disappears entirely and the patient appears calm and peaceful.

Other patients, however, are agitated because they are delirious. Some patients may have developed delirium either as an opioid side effect or in response to increasing blood levels of opioid as renal or hepatic function deteriorates. If the patient is expected to live for several more days, try lowering the opioid dose or changing the opioid and rehydrating her to decrease drug and metabolite levels. In addition, no matter what the underlying etiology of the delirium, if it is distressing the patient, try to control it with haloperidol (e.g., Haldol), olanzapine (Zyprexa, Zydis), or chlorpromazine. For patients with dyspnea, chlorpromazine, which is effective for both delirium and dyspnea, may be used as first-line therapy. Chlorpromazine is also more sedating than haloperidol, and this extra sedation may be beneficial at this time. Lorazepam (oral) or diazepam (rectal) can alleviate myoclonus; if the myoclonus is refractory to these agents and the IV route is available, use midazolam (titrated to effect).

Dyspnea. Dying patients with dyspnea benefit from the same symptomatic therapies recommended for patients with less advanced disease (see Table 9.5). Aggressive treatment of panic due to perceived breathlessness is particularly important for these patients, and hospice nurses often instruct families in how to administer the necessary morphine, chlorpromazine, or, for refractory panic, lorazepam.

Hydration. Although patients are unlikely to be thirsty or hungry, they may have a dry mouth caused by opioids or anticholinergic agents. A prospective study at St. Christopher's Hospice in London found no difference in the reports of thirst or dry mouth between dehydrated and normally hydrated dying patients (Ellershaw et al. 1995). Over 90 percent of all patients with these complaints were receiving opioids. In a report from Oregon, most hospice patients

PRACTICE POINTS: TREATMENT OF TERMINAL AGITATION

- Evaluate the patient for reversible physical problems: full bladder, fecal impaction, pain, nausea, hypoxia, secretions, opioid side effects (especially if there is decreased urine output), marked dehydration.
- Consider the need to change the drug regimen: opioid, opioid dose, or opioid preparation (e.g., from sustained to immediate release given as needed); decrease or discontinue anticholinergic medications; add lorazepam for anxiety for patients who can no longer take SSRIs, SNRIs, or gabapentin.
- Consider rehydration (1 to 1.5 liters / 24 hr).
- Consider the need for psychological or spiritual counseling (e.g., for resolution of family estrangements or for permission to let go).
- Medicate for anxiety
  —Lorazepam (e.g., Ativan), 1 mg p.o. or sublingual every 2 hours
- Medicate for mild delirium (see also Chapter 9).
  —Haloperidol (e.g., Haldol), 2 mg p.o., SQ, or IV, repeated at 30 minutes p.r.n. After an additional 30 minutes, double the dose, if needed, to a total of 20 mg / 24 hr.
  —Olanzapine (Zyprexa, Zydis), 2.5 to 5 mg p.o. b.i.d.; may give an additional 2.5 mg q4h p.r.n.
  —Chlorpromazine, 25 to 50 mg p.o. or p.r. every 4 to 8 hours; preferred for dyspneic patients or for those who would benefit from sedation.
- Palliative sedation for refractory delirium (see "Practice Points: Palliative Sedation").

PRACTICE POINTS: TREATMENT OF DYSPNEA THAT IS CAUSING PANIC

- Morphine, 5 to 10 mg liquid sublingual or p.o., 2–3 mg IV, or nebulized
- Chlorpromazine, 25 mg p.o. or p.r., or 12.5 mg IV
- Lorazepam, 1.0 mg sublingual, p.o. or IV

who voluntarily refused food and fluids to hasten their deaths seemed to their hospice nurses to have had a "good death," and they did not complain of hunger or thirst (Ganzini et al. 2003).

Parenteral hydration can actually cause increased distress by increasing urine output, inducing pulmonary or peripheral edema, or increasing ascites,

pulmonary secretions, or nausea and vomiting from increased gastric secretions. If you think parenteral hydration is indicated, try to limit replacement to a liter a day. A systematic literature review on hydration in the last weeks of life found mixed results: two studies showed less nausea and fewer physical signs of dehydration; two found adverse effects, such as increased ascites; and four showed no effect on problems such as delirium, thirst, or chronic nausea (Raijmakers et al. 2011). Moistening the mouth with gauze soaked in ice water or offering sips of water, ice chips, or fruit-flavored "Italian" ice is usually all that is needed.

PRACTICE POINTS: HYDRATION IN DYING PATIENTS

- Remember: thirst ≠ dehydration.
- Moisten lips with gauze soaked in ice water, or offer sips of water or plain or fruit-flavored ice chips.
- If parenteral hydration is chosen, do not exceed 1 to 1.5 liters/day to avoid increasing distress (e.g., increasing urine output, pulmonary secretions, nausea and vomiting, ascites, or pulmonary or peripheral edema).

Massive hemoptysis (or gastrointestinal bleeding). Massive hemoptysis is relatively rare, in one report occurring in 7 percent of about 500 patients hospitalized in a cancer hospital. In a dying patient, it will usually have been preceded by less extensive hemoptysis, giving you and the home care or hospice team the opportunity to prepare the patient and family. If you think the patient is likely to develop either a massive bleed (e.g., from a tumor of the head and neck or colon) or massive hemoptysis, suggest the family get dark-colored sheets, towels, and blankets to mask the blood. Because emergency intravenous access may be needed for patient sedation, consider insertion of a PICC line in patients without an indwelling venous access device.

The hospice nurse can leave a kit in the home that contains prefilled syringes of appropriate medications for a patient with massive hemoptysis or an exsanguinating bleed. It includes morphine, to be given intravenously when possible, and a benzodiazepine. Midazolam (Versed) can be given intramuscularly or intravenously; diazepam suppositories (e.g., Valium) can be given rectally. When the event occurs, the patient is placed bleeding side down, in the Trendelenburg position, and the medications noted above are given. If the nurses arrive in time, they can position the patient and administer these medications or start continuous infusions of morphine and/or midazolam, if necessary.

PRACTICE POINTS: TREATMENT OF MASSIVE HEMOPTYSIS OR EXSANGUINATING BLEEDING

- Ask the family to purchase dark-colored towels, blankets, or sheets to mask the blood.
- When appropriate, insert a PICC line for emergency IV access.
- Ascertain whether the family feels comfortable giving medications IV, SQ, or p.r. and instruct them as appropriate in administering the following:
  - —Rectal diazepam (10 mg), rectal lorazepam (2 mg), or IV midazolam (1 to 5 mg) from prefilled syringes.
  - —Morphine IV or SQ from prefilled syringes.
    Dose for opioid-naive patient: 10 mg morphine.
    Dose for patient on opioids: the intravenous equivalent of the rescue opioid dose.
    Example.
    For a patient taking 600 mg SR morphine every 24 hours:
    Oral rescue: 60 mg; IV rescue: 20 mg (i.e., 60 mg / 3).
    Opioid dose for sedation: 20 mg IV morphine.
- Teach the family how to place the patient bleeding side down in the Trendelenburg position when bleeding occurs.

Miscellaneous. For patients with urinary catheters who are experiencing dysuria, lidocaine can be added to saline bladder irrigation. For patients with nausea or vomiting due to bowel obstruction, continue octreotide and dexamethasone but decrease doses of metoclopramide when the renal function worsens; for nausea or vomiting from other causes, sublingual lorazepam (e.g., Ativan) or haloperidol (e.g., Haldol) can be effective as can specially compounded dexamethasone suppositories or commercial prochlorperazine suppositories. All these medications can be given in the home by the caregivers or by home care or hospice nurses.

Palliative sedation. Unfortunately, the doses of opioid, neuroleptic, or benzodiazepine that will control pain, cough, dyspnea, seizures, or agitation may sedate the patient so profoundly that unconsciousness ensues. Some ethicists have invoked the doctrine of double effect, discussed above, to support such "palliative sedation." They argue that although harm is foreseen, no harm is intended by the sedation-induced unconsciousness; on the contrary, the physician has an obligation to help the patient, and no alternative ways remain to provide that help. Since the action meets both these conditions (i.e., no harm is

PRACTICE POINTS: TREATMENT OF OTHER DISTRESSING PROBLEMS

- Catheter-induced dysuria: lidocaine bladder irrigation
- Nausea/vomiting
  - —Due to bowel obstruction: octreotide, 150 to 300 μg SQ b.i.d.
  - —Due to other causes: metoclopramide 30 mg + haloperidol 1.5 mg SQ or IV infusion over 24 hours
- Myoclonus due to opioid toxicity: lorazepam 1 mg sublingual, p.o., IV q4h prn; midazolam 5 mg loading dose (2 mg for patients over 60), then 10 to 100 mg / 24 hr IV infusion.

foreseen and benefit will accrue), palliative sedation may be considered ethical. Others cite the Autonomy of the patient and Beneficence as the ethical underpinnings.

Some have gone as far as suggesting that "death-hastening or death-causing palliative analgesic administration" is obligatory in such settings (Cavanaugh 1996). Situations may occur, Cavanaugh suggests, when our obligation to relieve the patient's pain or suffering is greater than our obligation to avoid hastening or causing death. In such instances, he says, the use of opioids or other agents to induce sedation would become obligatory.

Palliative sedation to unconsciousness. Palliative care experts consider using palliative sedation to unconsciousness when, despite their ongoing evaluation and management, a patient who is near death continues to experience intolerable physical, psychological, or spiritual/existential distress. This sedation is not a side effect of a medication given to relieve a symptom, such as the sedation induced by high doses of opioids for pain or dyspnea, or that induced by chlorpromazine for delirium. Here, sedation is the desired effect, and medications that induce sedation (e.g., midazolam, pentobarbital, or propofol) are used.

In the United States, there is legal and professional support for palliative sedation to unconsciousness. The United States Supreme Court (in *Vacco v. Quill* 521 U.S. 793 [1997]) recognized the right of patients to receive palliative sedation to unconsciousness if that is what is required to relieve their suffering at the end of life. The codes of ethics of the national professional societies of medicine, nursing, and pharmacy all have determined that the provision of palliative sedation to unconsciousness is consistent with ethical practice. When used in appropriate patients and carefully dosed, the sedation itself does not hasten death (Maltoni et al. 2012).

PRACTICE POINTS: PALLIATIVE SEDATION

- Indications: The patient is imminently dying and is experiencing suffering (physical, psychological, spiritual/existential) that is refractory to expert attempts at management, including palliative care and psychiatric and spiritual consultation. Whenever possible, two palliative care clinicians review the patient's case and document that palliative sedation to unconsciousness is the only remaining choice of therapy to relieve suffering. If the patient is in the hospital or a facility, the implementing physician reviews these indications with all the nurses and nurses' aides who work on the patient's floor and explores any moral or professional concerns. Consult ethics if needed.
- Family counseling:
  —Obtain informed consent from the patient and family or from the health care proxy.
  —Ask, "Later, will you still feel that we did the right thing? Will you feel that anything should have been done differently?"
- Initiate a medication regimen for reversible symptoms and titrate to comfort (e.g., pain: SQ or IV opioid infusions).
- If the patient is thought to be experiencing an ongoing symptom, continue the specific treatment for that problem while administering another agent. For example, opioids for pain, cough, or dyspnea; haloperidol for delirium.
- For distress that is refractory to specific therapies and counseling, choose one of the following initial doses and titrate to comfort. A physician must be present when the loading doses are given and the infusion is initiated and remain continuously present until the patient appears calm. Either a nurse or a physician can do the subsequent monitoring.
  —Midazolam
  Bolus 0.5 mg; then 0.5–1.5 mg/hr
  —Phenobarbital
  130 mg q 30 min to 1000 mg / 24 hr
  —Pentobarbital
  3 mg/kg load, then 1–2 mg/kg/hr
  —Thiopental
  3–5 mg/kg/hr

In 2013, the main area of controversy remained the use of palliative sedation in an imminently dying patient suffering from intractable existential distress alone (i.e., in the absence of refractory physical symptoms or delirium). Most professional clinical organizations in the United States (e.g., the American Medical Association, the American Nursing Association) exclude existential distress alone as a valid reason to give a dying patient palliative sedation to unconsciousness. The American Academy of Hospice and Palliative Medicine, however, does not specifically exclude palliative sedation for existential distress alone, and the Ethics Committee of the National Hospice and Palliative Care Organization was unable to reach consensus on whether it should be included (Kirk and Mahon 2010). Some noted ethicists, however, such as Dr. Eric Cassell, have argued that it should be allowed (Cassell and Rich 2010).

How would you recognize a patient suffering from existential distress? Consider the situation of Glen Smith, an 85-year-old patient with refractory leukemia and profound pancytopenia. He decided to discontinue blood product support and all antimicrobials. His oncologist expected him to die in a matter of days. Glen asked to be sedated: "I don't want to watch myself die." Glen had long ago said his good-byes to his family and friends, who supported his request. He had consulted with his pastor and knew that his spiritual beliefs did not preclude sedation prior to or at the time of death. But the hospital policy that allowed palliative sedation for refractory symptoms or delirium in imminently dying patients would not apply to Glen. He was discharged home, therefore, with hospice support, and his family told us that they were able to sedate him to his satisfaction using the lorazepam supplied in the hospice kit. He died peacefully three days later.

Most often, however, the consideration for palliative sedation to unconsciousness arises when a patient is suffering from refractory pain or other physical problem or from refractory delirium. In our facility, the palliative care team must be consulted. If chaplains or psychiatrists are not already seeing the patient, and we feel that would be helpful, we ask the team to consult them as well.

When clinicians have been doing their best, often for weeks, to bring the patient's suffering under control, they feel terrible when the suffering continues. Feelings of helplessness at being unable to lessen the patient's suffering may influence our choices about how to respond to a patient's request for hastened death or for sedation (Kelly et al. 2003; Schuman-Olivier et al. 2008). When we are considering instituting palliative sedation to unconsciousness, therefore, we always have an additional palliative care physician evaluate the patient, one who has not been part of the original consulting team. The goal of the second

palliative care physician is to try to determine whether there are any alternatives to palliative sedation to unconsciousness.

Whenever possible, we ask a senior, experienced physician for this second opinion. Both palliative care physicians must document their assessment of the patient, that sedation is the only means to relieve the patient's suffering, that the nurse manager of the unit and the patient's nurses agree, and that the patient and family have given informed consent to the sedation. See Figure 10.1 for an algorithm that describes the assessment and management that should precede consideration of palliative sedation to unconsciousness.

Discussions among the health care team, the patient, and family members usually achieve consensus on the need for and acceptability of sedation to unconsciousness as a means of achieving symptom control. Ethics consultants often facilitate our discussions, even when there is no overt disagreement among the health care team or between the team and the patient and family. They are able to provide another independent assessment of the proportionality of the treatment to the degree of suffering and reassure caregivers that their actions are indeed ethical. Patients must be DNR/DNI, and if the patient has an implanted

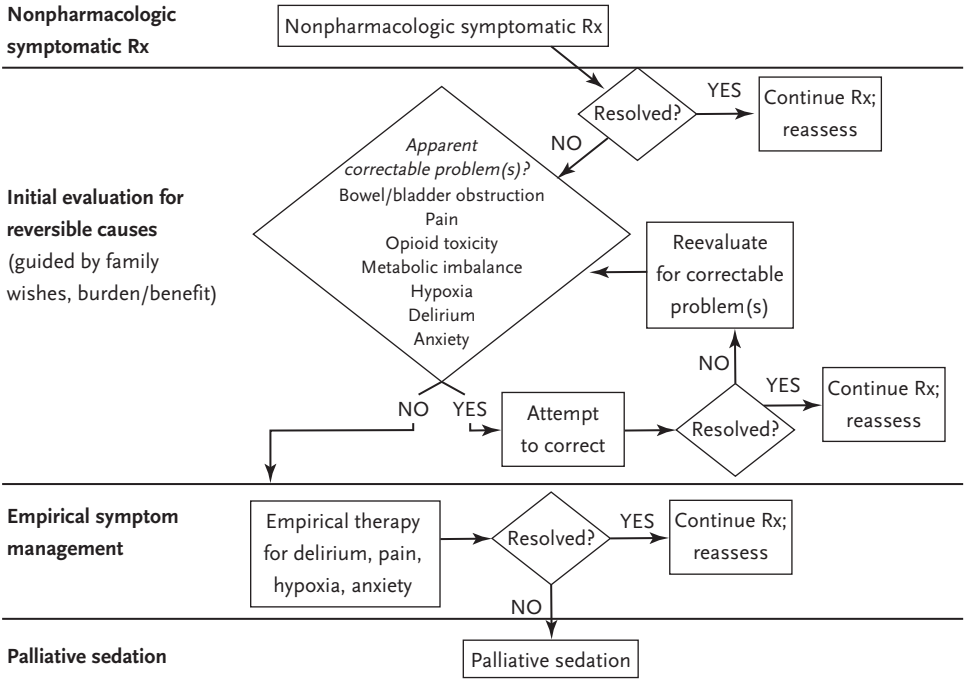

Figure 10.1. Agitation in the last days.

defibrillator, it must be inactivated. In most circumstances, we do not measure routine vital signs, and we turn off the monitors. We continue medications that provide comfort or control delirium.

Although there is no good evidence that sedation to unconsciousness itself hastens death (Maltoni et al. 2012), there is also no uniformity on whether artificial nutrition or hydration should be continued (Claessens et al. 2008). Retrospective reports indicate that 34 percent of patients died within 24 hours after initiation of palliative sedation to unconsciousness, and 96 percent died within one week, so discontinuing the hydration was not likely to have been the cause of these patients' deaths (Claessens et al. 2008). Some ethicists argue that if the patient is expected to survive more than two weeks, the cause of death would more likely be withholding hydration than the malignancy or other underlying cause of the patient's condition (Berger 2010). In those cases, families or patients might choose to continue hydration. We discuss with patients or their surrogate decision-makers (health care proxies) the burdens and benefits of continuing hydration or artificial nutrition. In my experience, no one has chosen to continue these.

In addition to the formal informed consent we obtain either from the patient or from the health care proxy, Dr. Byock (1997) recommends that we try to ensure that families will not regret their decision after the patient dies. He asks them to imagine that, several months after the death, they are recalling the events immediately preceding it and asking themselves whether anything should have been done differently. If the answer is no, he proceeds with the agreed-upon plan. He finds that families who have had these conversations do not develop subsequent guilt or regrets.

We use carefully monitored infusion of midazolam or pentobarbital to induce palliative sedation to unconsciousness (Schuman and Abrahm 2005) but others use propofol (Moyle 1995). Patients are usually comfortably sedated within an hour, and adjustments to the sedation are provided as needed, which is usually only during the first 24 hours. We continue careful monitoring for comfort until the patient dies.

Immediately after the Death

Studies indicate that many house officers are not trained in what to do after the patient dies (Ferris et al. 1998). If you are present at the death, or if you have been asked to "pronounce" the patient dead, offer your condolences to all others present before you leave the room. Such expressions can be very comforting. If you are invited to participate in a prayer, this is perfectly appropriate if you so wish. Encourage those present to spend as much time as they need to, to say or

do whatever they need to say or do, including touching the body. Answer the family's questions, and if the family was not present at the death, review the events preceding the patient's death with them. Reassure them about pain control or other concerns they have about the patient's suffering.

If hugging comes naturally to you and seems to be called for now, this, and the tears that may accompany it, are also OK. Just be sure to mitigate the manifestations of your sorrow so that the family doesn't feel the need to take care of you. Also offer condolences to the nurses and other staff who have cared for the patient. If the family has shared with you praise for the care that the patient received, be sure to share this with the staff as well: "*Her family told me they were so appreciative of the wonderful care you gave her.*" Those of you who work with house staff can help them deal with their grief by allowing them to review the circumstances of the death, their feelings for the patient, and their contributions to the care of the patient. Studies indicate that interns, in particular, need this support (Redinbaugh et al. 2003).

The nurses will be bathing and caring for the patient's body according to the patient's wishes. Some religions require special rituals after a person has died. These needs should be known prior to the death and arrangements made to have the appropriate people informed. Some Jewish patients, for example, will direct that their body be bathed and prepared for burial by a specially trained group of men or women (the Chevra Kadosha). In what follows, I discuss more about what you and the team can do to help the bereaved family.

What Our Institutions Can Do to Support Us

Before I review how we can help bereaved families, I want to say a word about what the hospitals we work in and your palliative care colleagues can do to support you. A survey of oncologists who were asked how their institutions could support them was published in 2012 (Granek et al. 2012). Oncologists, of course, are already engaged in working through their feelings about their many patients each year who die. Support from their office colleagues and staff and from friends and family, participation in religious observances or other spiritual practices, a good exercise routine, hobbies, and vacations (for those with the time) are all helpful.

But they are not enough. The oncologists reported that the hospitals they worked in could do much more to support them. They wanted training during fellowship on how to cope with their own losses, not just how to help patients and their families. They advocated for having mentors during training who modeled for fellows how to work through the feelings that are associated with patient deaths. Fact sheets and grand rounds could continue the education for

graduate physicians. Some wanted the hospital to host regular meetings in which they could normalize their feelings, share their stories, and debrief. They thought the hospital could provide a grief counselor or other mental health professional to whom they could go if more complex or painful concerns persisted.

Hospitals or other institutions that already have a palliative care team could involve them in supporting their oncology clinicians in all these areas. Palliative care clinicians can give talks, produce fact sheets, and teach oncology fellows through seminars or, better, through inpatient or outpatient clinical rotations. They can host a monthly meeting and create a safe space in which oncologists can share their stories, normalize their grief, and learn how to be better role models for their junior colleagues or trainees. Through these kinds of interactions, oncologists can begin to see their palliative care colleagues as resources between the meetings, when they see each other on the wards, or when there has been a particularly troubling case that the oncologist would really like to debrief with someone. In this way, palliative care clinicians can help prevent the compassion fatigue that results from unacknowledged or unprocessed grief (Abrahm 2012). As oncology clinicians learn ways to care for themselves, they will be much more helpful to the bereaved families they want to comfort.

The Bereaved

Our responsibilities to the patient and family continue after the patient's death, as we try to help the bereaved survivors. The suffering of the bereaved can manifest in many ways; for example, they are often sleepless, are at increased risk of developing major depression, and are at higher risk of committing suicide (Prigerson and Jacobs 2001). To anticipate their needs and to develop a suitable support program for them, it is useful to understand the many dimensions and manifestations of grief and mourning. The writings of Dr. Colin Parkes, Dr. Therese A. Rando, and Dr. Holly Prigerson are superb resources for physicians or other clinicians wanting in-depth, scholarly, and clinically useful discussions of normal and complicated mourning. Their work is based on research and practice in patients living in Western countries, and I have used their formulations as the foundation of the following discussion. References to their works, as well as to those of others working in this area, are listed at the end of the chapter.

Loss, Grief, and Mourning

Those who are bereaved are suffering from a number of losses. In addition to losing their loved one, secondary losses can occur, such as losing the medical

care team (Prigerson and Jacobs 2001), having to leave the family home, or changing one's social standing from wife to widow. In addition, the death is likely to revive the pain of losses that occurred many years before. A father's death, for example, may evoke memories of a divorce or the death of a child. The bereaved also suffer from the loss of "what might have been"—a reconciliation that never happened, a father to walk with down the aisle, a twenty-first birthday party. At the time of the death, bereaved family members enter this maelstrom of loss and may need help sorting out the sources of their pain.

A bereaved person's grief is a "process of experiencing the psychological, behavioral, social, and physical reactions to the perception of loss" (Rando 1993, p. 22). The intensity of a bereaved person's grief is predicated on several factors relating to the deceased and their relationship with the deceased, characteristics of the mourner, the nature of the death, and societal and cultural factors.

For example, being very attached to or very dependent on the deceased or having a great deal of ambivalence in one's feelings toward the deceased can exacerbate the grief, as can a personal history of clinical depression or difficulty in handling previous losses. A sudden or accidental death, suicide, or homicide also magnifies the grief experienced, while a good support system and religious rituals can lessen it.

Differentiation between grief and depression. It can sometimes be challenging to distinguish between manifestations of grief and those of depression (Block 2001; Prigerson et al. 1996). Grief is characterized by "intense feelings of sadness, yearning for the deceased, anxiety about the future, disorganization and feelings of emptiness" (Morris and Block 2012, pp. 272–73). But grieving people do not express the characteristics of depressed patients, which include "generalized feelings of hopelessness, helplessness, worthlessness, guilt, lack of enjoyment and pleasure, and active suicidal thoughts" (Morris and Block 2012, p. 274). People with grief do not have any plan to end their lives, can still get pleasure at times, and can look forward to the future. Crying is helpful for grieving people; people who are depressed do not seem to get any better after crying.

Depression responds better to pharmacologic therapy than does grief. Methylphenidate, SSRIs, and bupropion SR (sustained-release) all have been found to improve depression without worsening grief intensity (Block 2001; Zisook et al. 2001). For patients with prolonged grief disorder (see definition and discussion below), cognitive-behavioral therapy (CBT) with a therapist skilled with working with the bereaved may be helpful (Doka and Martin 2010; Greer 2010). Unfortunately, patients suffering from prolonged grief disorder do not improve with interpersonal psychotherapy or tricyclic antidepressants (Prigerson and Jacobs 2001). But paroxetine (Paxil) reduced symptoms by approximately 50 percent in

an open-label trial. These patients may also respond to a new type of psychotherapy that I discuss later in this chapter (Shear et al. 2005).

Styles of grieving. Each bereaved person's loss is unique, as are the experience and manifestations of the grief and mourning. Building on the work of Drs. Therese Rando, Colin Murray Parkes, William Worden, and others, Kenneth J. Doka, PhD, MDiv (professor of gerontology at the Graduate School of the College of New Rochelle and senior consultant to the Hospice Foundation of America), and Terry Martin, PhD (professor of psychology at Hood College), have published extensively about patterns of grief and mourning. Their book *Grieving Beyond Gender* (Doka and Martin 2010) sheds even more light on the causes of two distinct mourning styles, as well as on how we can recognize them in patients. The book is targeted to "grief counselors, psychologists, social workers, mental health counselors, pastoral counselors, and other therapists" (p. 4), but along with the theoretical discussions that would be of most interest to that group, I found clear descriptions of what they argue are the two most common types of functional grief and mourning, the "intuitive" and the "instrumental" styles.

A person who is aware of her feelings is likely to experience and manifest her grief and mourning in the intuitive style, which is different from the instrumental style of a person who is less in touch with her *feelings* but is very in touch with her *thoughts* about the events surrounding her loved one's death, and who normally evaluates, plans, and "does things" to decrease her pain when she is distressed. To illustrate the differences, consider Melinda and Winifred. They are housewives in their forties, each with two teenage children, both of whom lost their husbands unexpectedly two months ago.

Melinda has an intuitive pattern of grief and mourning. When we think of a grieving person, hers is the picture that usually comes to mind: she is likely to cry often, to need to share her grief with others, and to experience "intense inner pain, helplessness, hopelessness, and loneliness" (Doka and Martin 2010, p. 58). Melinda is eager to talk about her feelings, in a group or to a therapist; she wants help with her increased anxiety and with working on the emotional problems she is experiencing that seem to overwhelm her. She is distressed by her "prolonged periods of confusion, lack of concentration, disorientation, and disorganization" (p. 63). Her sister has moved in temporarily to help care for the children, since Melinda is unable to focus on that right now. And she has not even begun to think about learning to deal with financial matters.

Winifred is an instrumental griever. Her family thinks she is uncaring and wonder if she's experiencing any grief at all. She, like Melinda, is experiencing "prolonged periods of confusion, lack of concentration, disorientation, and disorganization"

which are frightening because they are completely foreign to her (p. 63). Instrumental grievers like Winifred have less intense feelings of grief and may even feel guilty and worried that they don't need to cry. Winifred, in fact, has not been crying, but she does have feelings of "sadness, anxiety, loneliness and yearning" (p. 66) that are not as strong or overwhelming as Melinda's. And unlike Melinda, Winifred's grief is triggered by *thoughts* about her lost husband and the times they shared together.

Also unlike Melinda, Winifred has been intensely concerned about the logistics and obligations that are now a part of her life. She is exhausted, partly because of the mental strain, and also because she has been staying up late nights bringing order out of what she is experiencing as chaos. While her family may not recognize it, Winifred is grieving by righting her world, not by talking about her grief.

Because of the way men and women are socialized in the United States, women are expected to be like Melinda: demonstrably emotional ("intuitive"), and men are expected to be the strong silent types, the "doers," who usually show more of an "instrumental" style of grief. As oncology clinicians, you see many people with "anticipatory grief" every day in your office. You've easily recognized the intuitive grievers. But if you and your staff are not familiar with the instrumental style of grieving, you may easily misinterpret the lack of overt emotion in a husband, wife, or partner of someone with far-advanced cancer as indifference. These instrumental grievers are grieving by providing meticulous care to their loved ones or by focusing on the tasks that need to be done for them. Harold might build a ramp for Maude's wheelchair so she can still get out of the house; Savannah might be taking care of Audrey's garden now that she cannot care for it herself. Harold and Savannah, of course, care just as much and need just as much support as people who grieve in the more easily recognized, intuitive style.

Gender is less of a determining factor in whether a person experiences and manifests the intuitive or instrumental style than are gender socialization, personality, and culture. Women are expected to show the intuitive style of grieving, but a man who grieves this way may have difficulty being supported at home or at work: he is supposed to "suck it up" and go on. Winifred, being a woman, is not supposed to grieve in the instrumental style, and her family misunderstands her actions and thinks she is even less caring than a man acting the same way would be perceived.

Most mourners are mixtures of intuitive and instrumental grievers. They find ways both to express their grief emotionally and to function within their new family roles or to return to their jobs. Problems can arise, of course, in either type of person who is unable to find any way to express her grief. I refer you to Doka and Martin for more in this area, including a discussion of dissonant responses to

grief, and of the roles of personality, gender socialization, and culture in shaping an intuitive or an instrumental style. The book also includes a discussion of other adaptive strategies mourners use, a chapter on self-help and interventions, and a Grief Pattern Inventory and instructions on how it should be scored.

Phases of grief and mourning, and processes of mourning. Although there is no set order, many people pass through one or more identifiable phases of grief and the rebuilding of a life without the deceased (Maciejewski et al. 2007). Sue Morris, a clinical psychologist who specializes in bereavement and is the director of Bereavement Services at DFCI, likens the pattern of grief to that of a wave in her 2008 book, *Overcoming Grief*. The intensity of the waves is greatest early in the course of the bereavement, and the amplitude generally decreases as time goes on (Morris 2008).

Dr. Therese Rando describes a useful framework for thinking about the processes of grief, which includes three phases of grief and mourning and six processes of mourning experienced by most of the bereaved, who are eventually able to reintegrate. Of course, not everyone experiences all these phases, but being familiar with them may help you understand the processes the bereaved survivors of your patients may be going through.

The phases, which include periods of overlapping manifestations, are *avoidance, confrontation,* and *accommodation,* as detailed in the box below (Rando 1993, p. 45).

During the *avoidance* phase, the bereaved person may initially appear numb, confused, or dazed, but some form of denial usually follows as the reality of the

PHASES OF GRIEF AND MOURNING, AND THE SIX "R" PROCESSES OF MOURNING

Avoidance Phase

1. *Recognize* the loss.
   Acknowledge the death.
   Understand the death.

Confrontation Phase

2. *React* to the separation.
   Experience the pain.
   Feel, identify, accept, and give some form of expression to all the psychological reactions to the loss.
   Identify and mourn secondary losses.

(continued)

3. *Recollect* and *reexperience* the deceased and the relationship.
   Review and remember realistically.
   Revive and reexperience the feelings.
4. *Relinquish* the old attachments to the deceased and the old assumptive world.

Accommodation Phase

5. *Readjust* to move adaptively into the new world without forgetting the old.
   Revise the assumptive world.
   Develop a new relationship with the deceased.
   Adopt new ways of being in the world.
   Form a new identity.
6. *Reinvest*

death intensifies. A wide range of behaviors can be expected, from uncontrolled shrieking to an unnerving calm.

During the *confrontation* phase, the pain intensifies because the absence of the person who has died asserts itself repeatedly. The mourner begins to yearn for the one who is dead, and waves of intense grief occur each time the deceased is sought and not found (Morris 2008); denial dissolves, and disorganization, depression, disinterest, and despair take its place (Parkes 1987). During this phase, the bereaved person commonly experiences various feelings, behaviors, physical symptoms, spiritual concerns, and thoughts (listed in Figure 10.2; for a more complete list of psychological, behavioral, social, and physical responses, see Rando 1993; Morris 2008; Morris and Block 2012).

The family must adjust to an environment without the person who has died. The role that the deceased played in the marriage, the family, and even the community may be increasingly revealed to the bereaved as time goes on, and mourning may be needed for each loss. Ideally, the bereaved will be able to cope with the increasing responsibilities, but many may need assistance or training—for example, in household finance or taking care of children.

Accepting the reality of the loss and experiencing its pain are essential if the pain is to be overcome. It is very difficult for people to move beyond loss if they never allow themselves to feel it in some way that is appropriate for them. Family obligations and unspoken strictures against demonstrations of grief can further impair a bereaved person's ability to experience the pain of the loss adequately.

WHAT TO EXPECT

Recovery from the loss of someone you love is often a long and painful process. However, if you can make it through the pain, things will get better. Most people find that their grief lasts anywhere from six months to two years. Since each person is unique, you will progress at your own pace and in your own way.

Grief is often associated with certain feelings and physical symptoms. Some of these include:

Common Feelings/Behaviors
- Fear and anxiety
- Anger and guilt
- Depression and despair
- Separation and longing
- Sudden wave of psychic pain
- Confusion and inability to concentrate or make decisions
- Tearfulness and crying
- Sighing
- Restlessness
- Yearning
- Helplessness
- Relief
- Hope

Spiritual Responses
- Faith may be strengthened, altered, or abandoned

Common Physical Symptoms
- Decreased or increased appetite
- Decreased energy; weakness of muscles
- Nausea and diarrhea
- Decrease or increase in your sex drive
- Inability to sleep or sleeping too much
- Feeling something stuck in your throat
- Tightness in chest, breathlessness
- Oversensitivity to noise
- Vivid dreams
- Dry mouth

Common Thoughts
- Disbelief
- Preoccupation with "if only" and "what if" and with memories
- Sense of his/her presence
- "Who am I now?"

WHAT TO DO

1. Give yourself permission to feel loss and to grieve over the loss.
2. Recognize that your grief is unique.
3. Expect to have some negative feelings.
4. Accept the help of others; let people know how they can help you.
5. Give yourself time alone.
6. Engage in physical activity.
7. Read books about feelings of grief and the process of recovery.
8. Talk to others about your loss.
9. Attend community support groups.
10. Most important: Recognize that at some point your pain will lessen.

WHAT NOT TO DO

1. Avoid making major changes.
2. Try not to withdraw from social activities.
3. Avoid excessive smoking or drinking.

WHEN TO CALL

Please call:
- If you have any questions or would like further information.
- If you feel that you would like professional counseling.

Figure 10.2. What to expect—for the bereaved. From J. Abrahm, M. E. Cooley, and L. Ricacho, Efficacy of an educational bereavement program for families of veterans with cancer, *Journal of Cancer Education,* 10:207–212, 1995; reprinted with permission.

Putting those feelings aside to deal with later or denying their existence altogether will only prolong or inhibit the process.

Eventually—and there is no useful timetable to determine when this will occur—most survivors reach *accommodation.* Dr. Rando chose this word carefully. It does not imply closure or return to the premorbid state. Instead, it suggests passage to a state in which life will never be the same, but in which bereaved persons tacitly acknowledge that an accommodation must be made if they are ever to resume old relationships and responsibilities. And even more difficult is the decision to try to establish new ones and risk recurrent loss, to realize that loving someone new need not mean betraying the memory of the person who has died. The bereaved person must craft a new relationship with the deceased, a new identity, and a new role in society.

Throughout the confrontation phase, and even in the accommodation phase and for years after the death, the bereaved are likely to experience what Dr. Rando calls "subsequent temporary upsurges of grief (STUGs)" (Rando 1993, p. 64). Precipitants for these recurrent pangs of grief (or "triggers" of a resurgent "wave" of grief [Morris 2008]) include anniversaries, holidays, and seasonal changes; reaching the age at which the loved one died; having a child reach the age of the child who died; favorite shared activities and personal reminders (e.g., music, smells, favorite objects); and a new personal or public trauma that resurrects the pain of old losses, especially if the one who died was the person turned to in times of crisis. The severity of the grief can match that of the initial loss and can be frightening for the bereaved, who had thought themselves beyond experiencing pain of that intensity.

Interventions

Given this understanding of what phases bereaved people are likely to experience, clinicians and researchers have devised interventions to ameliorate their suffering and have demonstrated the value of these interventions. Some take place in anticipation of the patient's death, as described in earlier chapters. These include skillfully communicating the diagnosis and terminal prognosis; providing emotional, psychological, and spiritual support as well as physical comfort; and helping families to resolve outstanding issues. It is also important to provide support in the final days and make the death as peaceful as possible.

Some patients may need cognitive-behavioral therapy (CBT) techniques to help them regain control. The bereaved can use Sue Morris's *Overcoming Grief* on their own or with the guidance of a therapist. *Overcoming Grief* is filled with

straightforward explanations of what the bereaved are likely to experience and when they should seek professional help. It offers insights into how to understand and help children who are grieving, helpful tips for those in any phase of grief, and several practical, easy-to-understand exercises that can help bereaved people find their way again after a significant loss.

Many of these exercises take the form of writing in a personal journal and answering specific questions that help elucidate thoughts and feelings so that the bereaved person can, with this new knowledge, allow new feelings and new behaviors to arise. When approaching painful emotions, such as regret, for example, Sue suggests that the bereaved person create a chart with five columns, A through E. Under A, the bereaved person writes the "Situation or trigger"; B—"Unhelpful thoughts"; C—"Feelings" (score/10) and "behavior" resulting from those feelings; D—"Helpful thoughts"; and E—"New feelings" (score/10) and "New behaviors" (that result from those feelings).

Sue gives us a sample chart written by a bereaved daughter experiencing a common cause of regret—she hadn't told her mother she loved her before leaving her that morning, and her mother died before she saw her again. In this chart (adapted from Lara's Diary Entry, Morris 2008, p. 79), the daughter completed the columns as shown in the box below.

SAMPLE BEREAVEMENT CHART

A. Situation or trigger	*B. Unhelpful thoughts*	*C. Feelings (score/10)*	*D. Helpful thoughts Behavior*	*E. New feelings (score/10) New behavior*
Thinking about mum's death	Why didn't I tell her I loved her that last time	Regret (9/10)	I did not know she was going to die. I can't predict the future.	Regret (5/10) Acceptance (5/10)
		Sobbing		Less crying

(From Morris 2008, by permission of the publisher)

Lara hadn't been aware that her regret, and the sobbing that accompanied it, was in response to a *thought*. The crying just seemed normal and spontaneous as she reflected about her mum's death; she wasn't aware of any intervening

thought that could have triggered her sobbing. But writing in the chart made that underlying connecting thought "visible," and once it was there, Lara could consider whether it was true or not. Once she could understand what she was blaming herself for, she could "think" her way to beginning to forgive herself, and she felt better.

Sue's book is full of many other similarly helpful exercises for coping with grief, moving forward to address difficult relationships, having difficult conversations, keeping that connection to the person you've lost, setting future goals, and more. The book can be used with or without the help of a social worker, a therapist, or a bereavement counselor. The bibliography is also likely to be helpful for people who are bereaved.

A Sample Bereavement Program

Hospice programs offer a formal bereavement program that takes place during the first year to 15 months after the patient's death; accommodation is usually well under way by the end of that time. After the formal program ends, the bereaved are welcome to continue participating in any bereavement activities that have been useful to them. Even families who are coping well benefit from support for this extended period after the patient's death. In addition, you might consider providing your own yearlong bereavement program. Various people in the office can participate, and it can be rewarding for each of them.

PRACTICE POINTS: SUPPORTING THE SURVIVORS

- Reassure family members that their response to the patient's death is normal.
- Listen sympathetically if they wish to review the circumstances of the patient's death.
- Reassure the family that you will remain available to them to help them with the grieving process.
- During the first year following the patient's death, call and write to the family at regularly scheduled intervals; don't wait for them to get in touch with you.
- Offer to send educational materials on manifestations of grief, coping techniques, and professional resources, if the family wishes.
- Invite them to participate in a memorial service.
- Identify family members at high risk for prolonged, intense grief and arrange a referral for professional support even before the patient dies.

At the time of death: the avoidance phase. When I still practiced oncology, we developed a bereavement program for our office. Our program began immediately after the death. Family members are often in a state of shock; their moods may swing wildly, changing from moment to moment. This volatility may be frightening for them—to be detached and numb one minute and distraught the next—and we tried to reassure them that this reaction is normal and that they should not worry about controlling themselves.

Now, when I am present at the death and meeting with the family, if I am sad, I let myself cry with them, or if they seem to need to talk things over, I ask leading questions to help them feel free to tell me their feelings. I find that they often want to review the circumstances of the death, to assure themselves that the person was not suffering and that everything that could have been done was done. I always try to find something for which I can praise them, such as their care of the patient or their advocacy role for him, and add how lucky he was to have had them there when he needed them. Even if I was not present at the death, when I call them later, I try to offer as much of this kind of reassurance and support as I can in the course of a telephone call.

Initial follow-up call. We called the family within 24 to 48 hours of the death to offer our condolences and help, and we still do this in our palliative care practice. During this call, we offer comfort and provide a listener for a retelling of the story of the death and the meaning of it for the bereaved. If necessary, we again reinforce the normality of the wide emotional swings or other symptoms of acute grief they may be experiencing. We listen empathetically and indicate our unconditional continued support. We also write them a letter, a sample of which is given in Figure 10.3. You and your house staff team can find a full discussion of the principles that underlie the writing of a good condolence letter in Fast Facts #022, 2nd edition, on the End of Life / Palliative Education Resource Center website (www.eperc.mcw.edu/FastFactsandConcepts).

If the family had been involved with a hospice program, we remind them that all members of the hospice team are still available to them. Some of the bereaved will have developed a close relationship with the hospice nurse, social worker, volunteer, or chaplain, and it may be easier for them to continue to work with someone familiar who knew the deceased.

Four to six weeks after the death; confrontation may displace avoidance. About a month after we send the letter, we call again and offer to send a variety of materials that we think might be helpful. We include a letter (Figure 10.3) and a list of readings, a description of grief, and a list of feelings and physical signs commonly experienced by those who are grieving, and what to do or not do about them (Figure 10.2).

Letter sent one week after death

Dear _____:
We share your sadness about your loss of _____ . We realize how hard it is when death occurs and want to let you know how important it is to be with family and friends at this time. If we can help you in any way, please call us at _____ . Again, all of us in the Hematology/Oncology department send our deepest sympathy.

Sincerely,

Letter sent three to six weeks after death and repeated at six months

Dear _____:
When we spoke on the phone, you said you would like more information to help you understand what you have been going through since _____ died. We have therefore enclosed information describing common feelings many people experience at the loss of a loved one as well as a list of books you could read that discuss these issues and a list of groups in your area that you could try for more support.

We realize that this is a hard time for you and we offer this information in the hope that it may be of some help. If you have any questions or want to talk with someone, please feel free to call us at _____ and ask for me.

Sincerely,

Holiday letter

Dear _____:
We were thinking of you because we know that this time of year may be difficult, since this is the first time without _____ . Others around you may also be thinking of _____ at this time. We want you to know that it is OK to talk about your loved one, of your memories of those special times together.

Remember to take one day at a time. If you find yourself feeling anxious, depressed or lonely, please feel free to call. We all hope you find comfort and peace at this time. If there's anything we can do to help, please call.

Sincerely,

Figure 10.3. Letters to the bereaved. From J. Abrahm, M. E. Cooley, and L. Ricacho, Efficacy of an educational bereavement program for families of veterans with cancer, *Journal of Cancer Education,* 10:207–212, 1995; reprinted with permission.

For example, at this point it is normal for bereaved family members or friends to experience sudden overwhelming grief, just as intense as it was initially, in response to familiar places or other reminders of the lost person (the "subsequent temporary upsurge of grief" or a "wave" of grief mentioned earlier). Alternatively, they may be angry about having been left or may become depressed, and they commonly experience a period in which they just don't care about anything.

We also include a list of support groups in their area, including those hosted by the hospice, because talking about their loss with skilled bereavement counselors, with others who have suffered similar losses, or with a bereavement support group can help in recovery. Groups such as Widow-to-Widow and, for parents who have lost a child, Compassionate Friends or Candlelighters (www.candle.org) can provide much-needed understanding and help with rebuilding a life. The circumstances of the death, or how the bereaved person was notified about it, may need to be repeated many times until the circumstances finally lose their ability to wound. The bereaved person may not feel comfortable "burdening" her friends or family with the story. But talking with a bereavement counselor or a therapist or with others in a similar situation, or attending a bereavement support group, may be acceptable and very helpful.

Other contacts. Because this has been shown to be a time of most need for bereaved families, we call again at six months and repeat our offer of various materials. Many families who have just begun the accommodation phase now find them helpful. We also participate in and help plan memorial services. And in anticipation of a recurrence of grief, we send a letter at the first anniversary of the person's death as well as a "holiday letter" (Figure 10.3) just before the winter holiday season, a few weeks before Thanksgiving. Bereaved survivors frequently respond to our offer to call and tell us how much they appreciate our continuing interest.

Initially we were somewhat concerned that these calls and letters might have an adverse effect, bringing up painful memories that had been successfully buried. But this was not the finding of a study we did to examine this question. A research nurse who had begun working with us after we started the program, and who did not know the patients or their families, conducted telephone interviews of the survivors, using a standardized questionnaire. She discovered that none of the survivors felt the interventions were harmful.

I think you and your staff will also find the process rewarding. You may find that as you speak to bereaved family members at longer and longer intervals, and begin to remember patients as they were before the terminal stages of their illness, it may help you to achieve closure and make it easier for you to move on.

Prolonged Grief Disorder

After the initial period of intense grieving, 80 to 90 percent of families do well (Morris and Block 2012). But the remainder do not. For these families, the bereavement process is severe and prolonged. Many do not pass beyond the avoidance phase. Others are unable to reach any kind of accommodation with their loss. Even though they have been bereaved for six months or longer, they experience daily or disabling intense yearning or searching for the deceased (Prigerson et al. 2009). In addition, they have several cognitive, emotional, and behavioral symptoms that cause significant impairments in their ability to function in, for example, the social, occupational, or domestic spheres.

These bereaved survivors have developed what is now termed "prolonged grief disorder" (Prigerson et al. 2009), an entity different enough from depression

FEATURES OF PROLONGED GRIEF DISORDER

Separation distress: The bereaved person experiences yearning daily or to a disabling degree and five or more of the following symptoms are experienced daily or to a disabling degree:

Cognitive, Emotional, and Behavioral Symptoms

1. Confusion about one's role in life or diminished sense of self (e.g., feeling that a part of oneself has died)
2. Difficulty accepting the loss
3. Avoidance of reminders of the reality of the loss
4. Inability to trust others since the loss
5. Bitterness or anger related to the loss
6. Difficulty moving on with life (e.g., making new friends, pursuing interests)
7. Numbness (absence of emotion since the loss)
8. Feeling that life is unfulfilling, empty, or meaningless since the loss
9. Feeling stunned, dazed or shocked by the loss

If these criteria are met, and the patient experienced the loss six months ago or longer, and if they cause significant impairment of physical, social, occupational or other area of function, the patient meets the algorithm's criteria for "prolonged grief disorder."

(From Prigerson et al. 2009)

(major depressive disorder), post-traumatic stress disorder, and generalized anxiety disorders, though it is not included in DSM-5 or ICD-10 (Prigerson et al. 2009). Symptoms of prolonged grief disorder can last for several years (Prigerson and Jacobs 2001). These persons are at increased risk for social dysfunction and various adverse health consequences (such as cardiac events, cancer, and hypertension).

Who is at risk? Several characteristics of the death itself, of the bereaved, and of their relationship with the deceased can predict whether a survivor is likely to remain reasonably functional or is at high risk for severe psychological distress (Rando 1993; Raphael 1977; Kissane and Zaider 2010; Zhang et al. 2006; Stroebe et al. 2007; Wright et al. 2010). Personal characteristics of bereaved survivors who are likely to be at high risk include having had a psychiatric disorder or separation anxiety as a child; poor social supports (or thinking that their support network is poor); abuse or neglect as a child; other stresses happening at the same time as the death; previous losses; having a very dependent relationship with the person who died or having conflict or unresolved issues at the time of the death; being present during a death that was apparently filled with suffering for the patient; and having a high level of distress immediately following the death (Morris and Block 2012).

Persons who were angry with or had an ambivalent relationship with the deceased may suffer "conflicted grief." At the time of the death, the survivor often feels nothing but relief, but months later, feelings of yearning, guilt, and loss become prominent. In contrast, persons with any of the other characteristics listed above may suffer "chronic grief": the grieving is as intense at the end of a year as it was initially; no effort has been made toward accommodation to a life alone.

Bereavement risk assessment tool. A tool, such as the Bereavement Risk Assessment Tool developed at St. Christopher's Hospice in London, can help you identify people who might be at high risk for a more troubled bereavement period (Figure 10.4). Families at high risk are those who score 15 or higher on this scale or those whom, for whatever reason, the evaluator suspects are likely to cope either badly (requiring special help) or very badly (requiring urgent help). For example, people who have many young children at home, who are burdened by feelings of anger and self-reproach, who do not work outside the home, or who are clinging or pining could easily score above 15 on this assessment tool.

Deaths that Prolong or Distort Normal Grief and Mourning

- Unexpected and sudden death, even in a patient with advanced disease
- Random, traumatic, violent, or mutilating death
- Death following a prolonged illness

PATIENT NAME _____ S/O NAME _____ DATE _____

A. Children <14 @ Home:	B. Occupation of Principal Wage Earner:	C. Anticipated Employment of Key Person:	D. Clinging or Pining:
0 None 1 One 2 Two 3 Three 4 Four 5 Five or more	1 Professional and executive 2 Semiprofessional 3 Office and clerical 4 Skilled manual 5 Semiskilled manual 6 Unskilled manual	0 Works full time 1 Works part time 2 Retired 3 Housewife 4 Unemployed	1 Never 2 Seldom 3 Moderate 4 Frequent 5 Constant 6 Constant, intense
E. Anger:	**F. Self-reproach:**	**G. Relationship Now:**	**H. How Person Will Cope:**
1 None (or normal) 2 Mild irritation 3 Moderate occasional outburst 4 Severe; spoils relationships 5 Extreme; bitter	1 None 2 Mild vague 3 Moderate 4 Severe 5 Extreme; major problem	1 Close, intimate 2 Warm supportive family 3 Family supportive but live a distance 4 Doubtful 5 None of these	1 Well; normal grief and recovery without special help 2 Fair; may need no special help 3 Doubtful; may need special help 4 Badly; requires special help 5 Very badly; requires urgent help

Figure 10.4. Bereavement Risk Assessment Tool. Total score >15 = high risk; score 4 or 5 on item H = urgent need. From C. Parkes and R. Weiss, *Recovery from Bereavement*, copyright © 1983 by Colin Murray Parkes and Robert S. Weiss; with permission of Basic Books, a member of Perseus Books, LLC.

- Death that seemed to be preventable
- Death of a child

Many who are bereaved after experiencing deaths with these characteristics exhibit what has been called the "unanticipated mourning" syndrome. Mourning is delayed or absent because denial is very strong, and survivors manifest symptoms typical of post-traumatic stress disorder. Such survivors have nightmares or hallucinations that replay the events preceding the death. They can experience anxiety or panic attacks in response to sights or sounds that remind them of the circumstances of the death.

Detecting prolonged grief disorder. Some of the bereaved who did not appear to be at high risk before the patient died will nevertheless manifest signs of prolonged grief disorder long after the death. Some people, for example, may remain in denial, having failed even to begin grieving: they may have never seemed sad and may even have avoided the funeral. Others are unable to make decisions; they lose initiative; they are filled with guilt and self-reproach, exhibit self-destructive behaviors, and may ultimately develop a major depression beginning at the time of the death and recurring at important anniversaries (Block 1985).

Still others are unwilling to let go, refusing to allow any of the deceased's personal effects to be moved. They cannot discuss their lost relative without becoming very upset; but they repeatedly talk about their bereavement and feel it acutely, even if months have elapsed. Finally, some may be intensely angry—at the deceased, at the physicians, or at others who cared for the person who died.

Treatment of patients with prolonged grief disorder. Clinicians and researchers who have done extensive work in this area recommend that, to minimize psychological morbidity, we begin psychological support for family members who are at high risk even before the patient dies. For those at less risk, we should maintain close contact after the death and institute intensive support as soon as they manifest a need.

Patients suffering from prolonged grief disorder are unlikely to respond, however, to standard antidepressant medications or to standard psychotherapy for depression, also referred to as interpersonal psychotherapy (IPT). There are encouraging data about a new treatment for these patients, called complicated grief therapy (CGT) (Shear et al. 2005). IPT focuses on grief and may also deal with the transition in roles the grieving person is experiencing or with disputes the bereaved had with the person who died. The hope of IPT is to help people develop a nuanced view of their relationship with the person who died, including both the positive and the negative aspects of that relationship.

CGT, in contrast, is based on the idea that the bereaved must focus on the loss itself, while creating new life goals that accommodate that loss. Importantly, people receiving CGT are asked to retell the story of the death, listen to themselves telling that story, and identify feelings of stress as they learn to confront and not avoid their feelings. The therapist asks the patient to have imagined conversations with the deceased and to revive both positive and negative memories.

Shear and colleagues (2005) compared IPT to CGT in a randomized controlled trial. An equal number of patients (about 27 percent in each arm of the study) were not able to complete the trial, but for different reasons. About half of those dropping out of the IPT arm were dissatisfied about its effectiveness, while

half of those leaving the CGT arm felt that telling the very distressing story would not be helpful to them. Therapists other than those delivering the PT or CGT assessed whether patients improved. In this study, CGT led to a significantly improved response rate ($p < .02$), with 51 percent of patients treated with CGT responding (95 percent confidence intervals, 37–65 percent) compared with 28 percent of patients treated with IPT (95 percent confidence intervals, 15–41 percent). Among those in each group who completed the trial, the findings were even more significant ($p<.006$), with 66 percent (95 percent confidence intervals, 50–82 percent) of those receiving CGT versus 32 percent (95 percent confidence intervals, 16–48 percent) of those receiving IPT responding.

Unresolved grief. For some bereaved—for example, those with unresolved anger, crises of faith, or guilt—ongoing spiritual counseling is helpful. For the unfortunate remainder, however, the grief seems never to lessen. These men and women are inconsolable. We must remember that their feelings are not their "fault." It may well be that the chemistry of their brains has changed, and their world is now radically different. They are heartbroken, and over time, some of them may find wisdom, if not ease, in their heartbreak.

To these people, I offer my continuing support and sympathetic ear. As well as I can, I bear witness. I listen to the stories they need to tell, try to understand their despair and the anger they need to express, and offer what small solace my attention can bring them. I understand that I am in a special position for them: I knew the person for whom they are grieving, and I may be the only one to whom they feel free to talk about their feelings. I neither judge them nor presume to urge them to "get over it." But if at some point they feel trapped by their grief or overwhelmed by it, and if, on their own, they begin to look for ways to find some balance in their lives, they may feel less inhibition about turning to me for the help they will then need.

The Telegram

The last service we can offer to patients and their families is to help the survivors recover from the loss. For a minority, support will be needed for the rest of their lives. The majority, however, will heal, and though they will never be quite the same, they will be able to integrate the loss into their new identity and role in society.

The courage demanded of the bereaved is eloquently captured by the writer Fred Chappell in his novel *I Am One of You Forever,* in the chapter "The Telegram." It is a story full of magic and truth, in which the telegram that announces a tragic death cannot be discarded or destroyed. We hear from the son in the family:

Then one evening I pulled a chair to the table and sat down to stare at the telegram. *Let it do to me what it can,* I thought. It was just at dusk and the telegram was the brightest object in the room. I don't know how long I sat looking. The room darkened and stars appeared in the upper window panes. At last the telegram began to change shape. Slowly wrinkling and furling inward, it took the form of a yellow rose, hand-sized, with a layer of glowing yellow petals. It seemed to hover an inch or so above the tablecloth. It uttered a mournful little whimper then, a sound I had once heard a blind puppy make when it could not find its mother's warm flank. And with that sound it disappeared from my sight forever, tumbled spiraling down a hole in the darkness. I watched it go away and my heart lightened then and I was able to rise, shaken and confused, and walk from the room without shame, not looking back, finding my way confidently in the dark.

I think that my grandmother and mother and father each had to undergo this ritual, and I think that we each saw the telegram take a different transformation before it disappeared, but we never spoke of that either.

By supporting family members as they find the strength to face their grief, we fulfill our last obligation to the deceased and to the family.

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Books

Palliative Care

Altilio, Terry, and Shirley Otis-Green. *Oxford Textbook of Palliative Social Work*. New York: Oxford University Press, 2011.

Benner, Patricia. *From Novice to Expert: Excellence and Power in Clinical Nursing Practice*. Menlo Park, Calif.: Addison Wesley, 1984.

Berger, Ann M., John L. Shuster, and Jamie H. von Roenn, eds. *Principles and Practice of Palliative Care and Supportive Oncology*, 4th ed. Philadelphia: Lippincott-Raven, 2013.
A superb text that includes useful reviews of all aspects of supportive oncology. It is particularly helpful for an American audience because the drugs recommended are available in the United States. It also offers very practical management suggestions and includes descriptions of the appropriate roles of invasive therapies for palliation. A must for every oncology fellowship program.

Billings, J. Andrew. *Outpatient Management of Advanced Cancer: Symptom Control, Support, and Hospice-in-the-Home*. Philadelphia: J. B. Lippincott, 1985.
An outstanding resource for clinicians. In addition to Part One's coverage of Symptom Control, Part Two, Psychosocial Support, and Part Three, Hospice-in-the-Home, present a unique, insightful approach to the concerns of dying patients and their families. Extensively referenced. (Out of print but copies available from some retailers.)

Breitbart, William, and Jimmie C. Holland, eds. *Psychiatric Aspects of Symptom Management in Cancer Patients*. Washington, D.C.: American Psychiatric Press, 1993.
Much of the information is this volume is included in the newer Oxford Textbook of Palliative Medicine *(listed below), but, as the title indicates, this 1993 book contains more information on specific psychiatric aspects. It is a clear, well-written volume. Of particular interest to those in primary care is the treatment of organic mental disorders and the chapter on the stress associated with caring for cancer patients.*

Bruera, Eduardo, Irene Higginson, Carla Ripamonte, and Charles von Gunten, eds. *Textbook of Palliative Medicine*. New York: Oxford University Press, 2006.
Excellent textbook for clinicians edited by some of the premier U.S. and international palliative care researchers and program leaders.

Buckman, Robert. *How to Break Bad News: A Guide for Health Care Professionals*. Baltimore: Johns Hopkins University Press, 1992.
An insightful guide to the conversations physicians have with patients and their families: why patients thought physicians said what they did, and why patients responded in the ways they did. Valuable to clinicians and educators as well as students.

Christakis, Nicholas A. *Death Foretold: Prophecy and Prognosis in Medical Care*. Chicago: University of Chicago Press, 1999.

Doyle, Derek, and D Jeffrey. *Palliative Care in the Home*. New York: Oxford University Press, 2000.

Faulkner, Anne, and Peter Maguire. *Talking to Cancer Patients and Their Relatives*. Oxford: Oxford University Press, 1994.

Gallagher-Allred, Charlotte R., and Madalon O'Rawe Amenta, eds. *Nutrition and Hydration in Hospice Care: Needs, Strategies, Ethics*. New York: Haworth Press, 1993 (paperback edition 1997).

A very clearly written, thorough discussion on the ethical, philosophical, and practical issues surrounding nutrition and hydration in patients who are near the end of life.

Glare, Paul, and Nicholas A. Christakis. *Prognosis in Advanced Cancer*. New York: Oxford University Press, 2008.

Brilliant discussions of the challenges of making and communicating prognoses; required reading for all who care for patients with advanced illness.

Hanks, Geoffrey W. C., Nathan Cherny, Nicholas A. Christakis, Marie Fallon, Stein Kaasa, and Russell K. Portenoy, eds. *Oxford Textbook of Palliative Medicine*. 4th ed. Oxford: Oxford University Press, 2010.

A comprehensive, thoroughly referenced, useful textbook on all aspects of palliative care and care of dying patients. A standard in the field.

Harper, Ralph. *On Presence: Variations and Reflections*. Philadelphia: Trinity Press International, 1991.

For readers interested in a more philosophical and spiritual discussion of presence.

Holland, Jimmie C., William S. Breitbart, Paul B. Jacobsen, Marguerite S. Lederberg, Matthew Loscalzo, and Ruth McCorkle. *Psycho-oncology*. 2nd ed. New York: Oxford University Press, 2010.

This comprehensive text is an excellent resource for those interested in various aspects of psychological care, not only of patients and their families, but of the medical personnel who care for them (nurses, house staff, and so on).

Houldin, Arlene D. *Patients with Cancer: Understanding the Psychological Pain*. Philadelphia: Lippincott, 2000.

Dr. Houldin is an insightful clinician who shares the lessons she has learned from years of counseling cancer patients.

Maguire, Peter. *Communication Skills for Doctors*. New York: Oxford University Press, 2000.

These books contain superb descriptions of the components of conversations that nurses and physicians must have with cancer patients. They are full of useful suggestions for how to deepen and improve these conversations so that we can discern what is troubling our patients and their families.

Meier, Diane M., Stephen L. Isaacs, Robert G. Hughes, eds. *Palliative Care: Transforming the Care of Serious Illness*. San Francisco: Jossey-Bass, 2010.

A collection of seminar papers on palliative care from the MacArthur-winning creator of the Center for Palliative Care (CAPC), Dr. Diane Meier, and her colleagues.

Rauch, Paula, and Anna Muriel. *Raising an Emotionally Healthy Child When a Parent Is Sick*. A Harvard Medical School Book. New York: McGraw-Hill, 2006.

Rolling Ferrell, Betty, and Nessa Coyle, eds. *Oxford Textbook of Palliative Nursing.* 3rd ed. New York: Oxford University Press, 2010.
A state-of-the art discussion of the subject; required for all hospital and palliative care program libraries.

Saunders, Cicely, Mary Baines, and Robert Dunlop. *Living with Dying: A Guide to Palliative Care.* 3rd ed. Oxford: Oxford University Press, 1995.
In just 56 pages, Dame Cicely, the founder of the modern hospice movement in England, provides a splendid overview of the essential elements of caring for dying cancer patients, their families, and the staff responsible for them.

Stone, Douglas, Bruce Patton, and Sheila Heen. *Difficult Conversations: How to Discuss What Matters Most.* 2nd ed New York: Penguin Books, 2010.
The lessons of this book, written for businesspeople by the group who wrote Getting to Yes, *are highly applicable to the conversations that must be undertaken in palliative care.*

Wolfe, Joanne, Pamela S. Hinds, and Barbara M. Sourkes. *Textbook of Interdisciplinary Pediatric Palliative Care.* Philadelphia: Elsevier Saunders, 2011.
This is the first textbook of pediatric palliative care, edited by pioneer clinicians and researchers in the field.

Pain and Symptom Management

Andrews, Tom. *The Hemophiliac's Motorcycle.* Iowa City: University of Iowa Press, 1994.
Eloquent evocations and narrative poems telling what it was like growing up with hemophilia in the pre–home care era, and then living in the peri-HIV era.

Barber, J., ed. *Hypnosis and Suggestion in the Treatment of Pain: A Clinical Guide.* New York: W. W. Norton, 1996.
This book includes an orientation to hypnotic evaluation and a discussion of the use of hypnosis in pain syndromes (including cancer pain) and in children and elders.

Fishman, Scott M., Jane C. Ballantyne, James P. Rathmell, eds. *James P. Bonica's Management of Pain.* 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2010.
The editors, leading pain researchers and clinicians, have updated Bonica's classic work without losing any of its thorough, scholarly, and practical focus.

McMahon, Stephen, Martin Koltzenburg, Irene Tracey, and Dennis C. Turk, eds. *Wall & Melzack's Textbook of Pain.* 6th ed. New York: Churchill Livingstone, 2013.
An exhaustive textbook, authoritative and wide ranging in scope, first edited by Melzack and Wall, two original thinkers who are among the modern founders of the field of pain research and management.

Smith, Howard S., ed. *Current Therapy in Pain.* Philadelphia: Saunders, Elsevier, 2009.
Concise, practical coverage of managing pain both of cancer and non-cancer origin.

Smith, Howard S., and Setven D. Passick, eds. *Pain and Chemical Dependency.* New York: Oxford University Press, 2008.
Oncology clinicians will find this book helpful in understanding and managing patients with cancer pain and active or past substance abuse histories. Both Drs. Smith and Passik have worked with countless cancer patients and their families who are facing these challenges, and they share their wisdom in this volume.

Death and Dying

Blank, Linda L., ed. *Caring for the Dying: Identification and Promotion of Physician Competency*. Philadelphia: American Board of Internal Medicine, 1996.

Byock, Ira. *Dying Well: Peace and Possibilities at the End of Life*. New York: Riverhead Books, 1997.

Dr. Byock is a past president of the American Academy of Hospice and Palliative Medicine. In this book, he uses the narratives of the patients and families he has cared for to explore the possibilities for growth even at the end of life.

Byock, Ira. *The Four Things That Matter Most: A Book about Living*. New York: Free Press, 2004.

Expanding on themes raised in Dying Well, *Dr. Byock offers a continued meditation on how families and patients can communicate the important things to each other when the patient's time is short.*

Callahan, Daniel. *The Troubled Dream of Life*. New York: Simon & Schuster, 1993.

Dr. Callahan, of the Hastings Center, explores our "illusion," as he calls it, of control regarding our choices of how we die—our medical options, euthanasia, and "the pursuit of a peaceful death." He urges us to reframe how we perceive death—accepting it as a part of nature, rather than regarding it as a moral evil to be fought at any cost.

Corless, Inge B., Barbara B. Germino, and Mary A. Pittman. *A Challenge for Living: Dying, Death, and Bereavement*. 2nd ed. New York: Springer, 2005.

A compilation of essays by leaders in various disciplines on the physical, psychosocial, and spiritual needs of the patient and the caregivers, as well as the needs of the bereaved. Each essay is referenced.

Curtis, J. Randall, and Gordon D. Rubenfeld, eds. *Managing Death in the Intensive Care Unit: The Transition from Cure to Comfort*. Oxford: Oxford University Press, 2001.

Dr. Curtis and colleagues have written a very useful series of essays that deal with the ethical and practical aspects of caring for dying patients in the ICU.

Diamant, Anita. *Saying Kaddish: How to Comfort the Dying, Bury the Dead, and Mourn as a Jew*. New York: Schocken Books, 1998.

Halifax, Joan. *Being with Dying: Cultivating Compassion and Fearlessness in the Presence of Death*. Boston: Shambhala, 2008.

Roshi Joan Halifax, a Buddhist teacher and scholar, is known for her retreats in which she teaches clinicians and laypeople alike how to be in the presence of death. This book is a helpful introduction to her work.

Kuhl, David. *What Dying People Want: Practical Wisdom for the End of Life*. New York: Public Affairs, 2002.

Lief, Judith L. *Making Friends with Death: A Buddhist Guide to Encountering Mortality*. Boston: Shambhala, 2001.

Mojtabai, A. G. *Soon: Tales from Hospice*. Cambridge, Mass.: Zoland Books, 1998.

Parkes, C. M., and H. G. Prigerson. *Bereavement: Studies of Grief in Adult Life*. 4th ed. New York: Routledge, 2010.

Parkes, C., and R. Weiss. *Recovery from Bereavement*. New York: Basic Books, 1983.

These books and that written by Therese Rando, listed below, provide clinicians with comprehensive discussions of bereavement and of the treatment of those who cannot seem to recover from the patient's death.

Quill, Timothy E. *Death and Dignity.* New York: W. W. Norton, 1993.

A thought-provoking book by the noted advocate of palliative care, patient dignity, and the patient's right to die. Chapters include Making Choices and Taking Charge, Reconsidering Medicine's Goals and Values, Medical Technology, Comfort Care and Its Limits, Physician Assisted Suicide, and Advance Directives. Includes a bibliography.

Rando, Therese A. *Treatment of Complicated Mourning.* Champaign, Ill.: Research Press, 1993.

This book and that written by C. Parkes and R. Weiss, listed above, provide clinicians with comprehensive discussions of bereavement and of the treatment of those who cannot seem to recover from the patient's death.

General Interest

American Cancer Society. *Guidelines on Support and Self-Help Groups.* Atlanta: American Cancer Society, 1995.

A practical, working manual for those interested in developing various types of support or self-help groups sponsored by the American Cancer Society. Evaluation tools and references are included.

Atul, Gawande. *Complications: A Surgeon's Notes on an Imperfect Science.* New York: Picador, 2002.

A beautifully written book full of insight from a superb physician and teacher. This was the first, but if you like it, read all his books!

Aulisio Mark P., Robert M. Arnold, and Stuart J. Younger, eds. *Ethics Consultation: From Theory to Practice.* Baltimore: Johns Hopkins University Press, 2003.

A valuable resource for institutions that wish to train ethics consultants and start ethics committees. Of particular utility is the chapter on core competencies for health care ethics consultation.

Bandeira, Manuel. *Selected Poems.* Edited and translated by David R. Slavitt. Riverdale-on-Hudson, N.Y.: Sheep Meadow Press, 2002.

Poems of love and death.

Bigby, Judyann, ed. *Cross-Cultural Medicine.* Philadelphia: American College of Physicians, 2003.

A well-written and well-edited contemporary account of the issues that must be considered as clinicians care for patients from the variety of cultures within the United States. The book includes, but is by no means limited to, discussions on communicating about the illness and its prognosis and rituals surrounding dying patients.

Boethius. *The Consolations of Philosophy.* Translated by David R. Slavitt. Cambridge, Mass.: Harvard University Press, 2008.

From the publisher's notes: "Written under a death sentence. Boethius (c. 480–524), an Imperial official under Theodoric, Ostrogoth ruler of Rome, found himself, in a time of political paranoia, denounced, arrested, and then executed two years later without a trial. Composed while its author was imprisoned, cut off from family and friends, it remains one of Western literature's most eloquent meditations on the transitory nature of earthly belongings, and the superiority of things of the mind."

Broyard, Anatole. *Intoxicated by My Illness.* New York: Fawcett Columbine, 1992.

Anatole Broyard, journalist and author, died of metastatic prostate cancer. This moving, lively collection of articles deals with multiple subjects of interest to physicians, including what he expected from his own physicians, as well as a discussion of other books about cancer. It also includes a short story that mirrors Broyard's experience as one of his parents died of cancer.

Cancer Care. *A Helping Hand: The Resource Guide for People with Cancer*, 2nd ed. Available from Cancer Care, 1180 Avenue of the Americas, New York, NY 10036-3602; telephone: 800-813-HOPE (4673) or 212-221-3300; e-mail: info@cancercare.org; website: www.cancercare.org.

A comprehensive and detailed listing of the growing number of services available across the country to people with cancer. In addition to the addresses, telephone and fax numbers, and e-mail addresses for hundreds of resources for people with cancer, each organizational listing contains a description of its mission and the services it provides.

Cassell, Eric J. *The Healer's Art*. Cambridge, Mass.: MIT Press, 1976.

Cassell, Eric J. *The Nature of Healing: The Modern Practice of Medicine*. New York: Oxford University Press, 2013.

Cassell, Eric J. *The Nature of Suffering and the Goals of Medicine*. 2nd ed. New York: Oxford University Press, 2004.

Seminal works from a physician and scholar who elucidates the unspoken assumptions that impede successful care of the dying in America today. He analyzes the structural, personal, and professional barriers that separate us from our patients and prevent us from understanding and appreciating their goals and values. He comprehensively yet concisely delineates the nature of suffering and the sources of healing. All physicians caring for patients with acutely disabling or chronically advanced illness will benefit from the insights they can gain from these books.

Cassileth, Barrie R. *The Complete Guide to Complementary Therapies in Cancer Care: Essential Information for Patients, Survivors and Health Professionals*. Hackensack, N.J.: World Scientific Publishing, 2011.

Most oncology patients are using one or more complementary therapies along with the antineoplastic therapies oncologists prescribe. They appreciate a chance to discuss these therapies and their risks and benefits with their oncology team members. Dr. Cassileth is an internationally known expert on complementary medicine. As her bio states: "Dr. Cassileth is the Laurance S. Rockefeller Chair and Chief of the Integrative Medicine department at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City. She has an extensive medical leadership career and is a foremost authority on evidence-based complementary therapies in oncology. She is a staunch opponent to 'cancer quackery.' Her work includes 180 publications in the medical literature, 46 medical textbook chapters, 11 authored books, and 12 publications for physicians, patients and families. She was a founding member of the Advisory Council to the U.S. National Institutes of Health Office of Alternative Medicine, now the National Center for Complementary and Alternative Medicine. She is Founding President of the Society for Integrative Oncology." This book is an extremely valuable reference tool for those of us working with patients who seek these therapies in addition to those we offer—Dr. Cassileth suggests that this includes at least one-third to one-half of cancer patients.

de Sponde, Jean. *Sonnets of Love and Death*. Edited and translated by David R. Slavitt. Evanston, Ill.: Northwestern University Press, 2001.

Field, M. J., and C. K. Cassell, eds. *Approaching Death: Improving Care at the End of Life*. Washington, D.C.: Institute of Medicine, National Academy Press, 1997.

Gilbert, Sandra M. *Death's Door: Modern Dying and the Ways We Grieve*. New York: WW Norton and Company, 2006.

Hall, Donald. *Without*. New York: Houghton Mifflin, 1998.

Lynch, Thomas. *The Undertaking: Life Studies from the Dismal Trade*. New York: Penguin Books, 1997.

Pastan, Linda. *Carnival Evening: New and Selected Poems, 1968–1998*. New York: W. W. Norton, 1998.

The poem "The Five Stages of Grief" is of special interest to those of us trying to understand how to help our bereaved patients.

Price, Reynolds. *A Whole New Life: An Illness and a Healing*. New York: Atheneum, 1994.

A cautionary tale for physicians by novelist and short story writer Reynolds Price, who had locally advanced cancer; he chastises us for what he terms our "clinical distance."

Remen, Rachel Naomi. *Kitchen Table Wisdom: Stories that Heal*. New York: Riverhead Books, 1996.

Remen, Rachel Naomi. *My Grandfather's Blessings: Stories of Strength, Refuge, and Belonging*. New York: Riverhead Books, 2000.

Rachel Remen is co-founder and medical director of the Commonweal Cancer Help Program. She has extensive experience in the clinical care of those who are suffering and facing life-threatening illnesses as well as in teaching undergraduate, graduate, and practicing physicians how to heal the pain of their own losses—and to become better physicians in the process. In both of these readable, engaging books, she uses stories that teach by indirection and powerfully convey her message.

Roth, Philip. *Patrimony*. New York: Simon & Schuster, 1991.

A wonderful revelation of Philip Roth's relationship with his father—their time together when Roth was a child and the years in which his father's life was profoundly altered by a rare brain tumor. Roth was the primary caregiver for his father during this time, and he writes about the experience as only he can.

Stone, John. *Where Water Begins: New Poems and Prose*. Baton Rouge: Louisiana State University Press, 1998.

Sulmasy, D. P. *The Healer's Calling: A Spirituality for Physicians and Other Health Care Professionals*. New York: Paulist Press, 1997.

Daniel Sulmasy is a philosopher, a health services researcher, a Franciscan friar, and a medical oncologist. In this eloquent, thoughtful book he relates his "personal experience of being a man of faith engaged in the work of a health care professional" as a basis for our own self-explorations. Chapters include Spirituality and the Health Care Professional; Medicine, Love and the Art of Being Uncertain; The Wine of Fervent Zeal and the Oil of Compassion; God-Talk at the Bedside; Prayer and the Five Senses: A Physician's Meditation; Suffering, Spirituality, and Health Care; and Wounded Healers.

Taylor, Jill Bolte. *My Stroke of Insight: A Brain Scientist's Personal Journey*. New York: Viking, 2008.

An astonishingly clearly written account by a neuro-anatomist of her experience with a left hemisphere stroke and her path to recovery. Unique insights in how to speak with and how to help such patients.

Webb, Marilyn. *The Good Death: The New American Search to Reshape the End of Life.* New York: Bantam, 1997.

Marilyn Webb is an investigative journalist who spent six years exploring this topic. In this almost 500-page volume, she shares the stories of patients and families for whom death provided either the opportunity for growth or unremitting pain and explains the many factors that contributed to such different outcomes.

Other Books of Interest

Annas, G. J. *The Rights of Patients: The Authoritative ACLU Guide to Patient Rights.* An American Civil Liberties Union Handbook. 3rd ed. Carbondale: Southern Illinois University Press, 2004.

Benson, Herbert, with Marg Stark. *Timeless Healing: The Power and Biology of Belief.* New York: Scribner, 1996.

Chochinov, Harvey M., and William Breitbart, eds. *Handbook of Psychiatry in Palliative Medicine*. 2nd ed. New York: Oxford University Press, 2009.

Jonsen, A. R., M. Siegler, and W. J. Winslade. *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine.* 7th ed. New York: McGraw-Hill, 2010.

Handbooks, Primers, and Guidelines

Palliative Care

Hallenbeck, J. L. *Palliative Care Perspectives.* Oxford: Oxford University Press, 2003.

National Consensus Project for Quality Palliative Care. *Clinical Practice Guidelines for Quality Palliative Care.* 3rd ed. Alexandria, Va.: NHPCO, 2013. NHPCO Marketplace, Dept. 929, Alexandria, VA 22334-0929; telephone: 800-646-6460; website: www.nhpco.org/marketplace.

Oneschuk, Doreen, Neil Hagen, and Neil MacDonald, eds. *Palliative Medicine: A Case-Based Manual.* 3rd ed. Oxford: Oxford University Press, 2012.

This book is designed for physicians who wish to teach principles of palliative medicine to medical students, residents, or fellows. Thirty symptom problems and psychosocial issues are addressed in carefully designed cases, along with relevant references.

Quill T, Holloway R, Shah M, et al. 2010. *Primer of Palliative Care.* 5th ed. Glenview, Ill.: American Academy of Hospice and Palliative Medicine. Available from American Academy of Hospice and Palliative Medicine: telephone: 703-787-7718; e-mail: aahpm@aahpm.org; website: www.aahpm.org.

A useful primer for managing the most distressing symptoms: pain, dyspnea, nausea and vomiting, anorexia, constipation, restlessness and delirium, and psychological, social, and spiritual distress. It contains a useful annotated bibliography of key references.

Stahl, Bob, and Elisha Goldstein. *A Mindfulness-Based Stress Reduction Workbook*. Oakland, Calif.: New Harbinger, 2010.

An easy-to-use workbook with extremely compelling meditations for clinicians on impermanence, anxiety and stress, and other issues. Includes an MP3 CD with 21 guided meditations. Terrific aid to a self-care practice.

Waller, Alexander, and Nancy L. Caroline. *Handbook of Palliative Care in Cancer.* Boston: Butterworth-Heinemann, 1996.

An extremely well-organized, useful, inexpensive handbook containing clear, succinct recommendations for evaluation and treatment of the multitude of physical and emotional symptoms experienced by patients with cancer. An excellent addition to the library of any clinician caring for cancer patients. Referenced.

Pain

American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 6th ed. Chicago: American Pain Society, 2008. Available from American Pain Society 8735 W. Higgins Road, Suite 300. Chicago, IL 60631-1485.

Miaskowski, C., J. Cleary, R. Burney, et al. *Guideline for the Management of Cancer Pain in Adults and Children.* APS Clinical Practice Guidelines Series, No. 3. Glenview, Ill.: American Pain Society, 2005. www.ampainsoc.org.

This landmark publication is a consensus document prepared by the leading national pain experts from numerous clinical fields. It contains assessment and management guidelines, including pharmacologic and nonpharmacologic techniques, guidelines for treating the elderly, and assessment and management tools.

Death and Dying

Aries, Philippe. *The Hour of Our Death: The Classic History of Western Attitudes toward Death over the Last One Thousand Years.* New York: Knopf, 1981.

Lynn, Joanne, Joan Harrold, and Janice Lynch Shuster. *Handbook for Mortals: Guidance for People Facing Serious Illness.* 2nd ed. New York: Oxford University Press, 2011.

A straightforward, clearly written manual that I give to patients and families who are facing a terminal prognosis. It includes practical suggestions and seeks to empower families to get the information they need from their health care providers. It is a valuable book also for nurses and physicians who are not familiar with the demands that caring for these patients place on them and on families as they try to navigate the health care system and care for the patients at home.

Parkes, Colin Murray, Pittu Laungani, and Bill Young, eds. *Death and Bereavement across Cultures.* New York: Brunner-Routledge, 1997.

In the editors' words, this handbook "describes the rituals and beliefs of the major world religions; explains their psychological and historical context; shows how customs are changed by contact with the West; and considers the implications for the future." It also includes an exploration of mourning traditions throughout the world.

Series

American Academy of Hospice and Palliative Medicine and UNIPACS. *Hospice/Palliative Care Training for Physicians: A Self Study Program.* 4th ed. Dubuque, Iowa: Kendall/Hunt Publishing, 2013. Available from AAHPM, e-mail: aahpm@aahpm.org.

This nine-part UNIPAC series offers an excellent, modular, case-based study program for those interested in learning more about palliative care. Pre- and post-tests are included, and CME credit is available for each module. Volumes include: (1) The Hospice and Palliative Medicine Approach to Care; (2) Alleviating Psychological and Spiritual Pain; (3) Assessing and Treating Pain; (4) Managing Non-pain Symptoms; (5) Communication and the Interdisciplinary Team; (6) Ethical and Legal Dimensions of Care; (7) Caring for Patients with HIV/AIDS; (8) Caring for Pediatric Patients; and (9) Caring for Patients with Chronic Illnesses. Modules can be purchased individually or in sets (for a discount).

Bruera, Eduardo, and Russell K. Portenoy, eds. *Topics in Palliative Care*. 4 volumes. Oxford: Oxford University Press, 1997, 1998, 1998, 2000.

Bruera, Eduardo, and Russell K. Portenoy, eds. *Issues in Palliative Care Research (Medicine)*. New York: Oxford University Press, 2003.

Journals

These journals and newsletters are for physicians interested in practical, useful articles discussing improvements in symptom management or palliative care–related subjects. Authors include clinicians from various medical and other clinical disciplines.

Alternative Medicine Alert. American Health Consultants, P.O. Box 71266, Chicago, IL 60691-9986; telephone: 800-688-2421; fax: 800-850-1232.

The Journal of Pain and Symptom Management. Russell K. Portenoy, editor. Elsevier Science, 655 Avenue of the Americas, New York, NY 10010; telephone: 800-437-4636; fax: 212-633-3680; e-mail: usinfo-f@elsevier.com. Official journal of the American Academy of Hospice and Palliative Medicine.

Journal of Palliative Medicine. Charles von Gunten, editor-in-chief. Mary Ann Liebert, 2 Madison Avenue, Larchmont, NY 10538; telephone: 914-834-3100; fax: 914-834-3582; website: www.liebertpub.com.

Palliative Medicine. Catherine Walshe, editor-in-chief. Sage, 1 Oliver's Yard, 55 City Road, London, EC1Y ISP, UK; telephone: +44 (0)20-7324-8601.

Supportive Care in Cancer. F. D. Ashbury, editor-in-chief. Springer Verlag, 233 Spring Street, New York, NY, 10013-1522; telephone: 800-977-4643; fax: 212-460-1700; e-mail: journals-ny@springer.com; website: www.mascc.org. Official journal of the Multinational Association of Supportive Care in Cancer. This journal is the best source for research studies of novel supportive care in cancer patients.

Patient Education Materials for Clinicians

American Society of Clinical Oncology: Cancer Net.

Cancer.Net *is the ASCO website for patients that provides downloadable publications on multiple symptom management, palliative care, communication, and advance care planning topics. These can be provided to patients as needed at the time of office visits or mailed in preparation for discussions about these topics during an office visit.*

ASCOanswers. Advanced Cancer Care Planning: A Decision-Making Guide for Patients and Families Facing Serious Illness. Alexandria, Va.: ASCO, 2013.

This handbook from ASCO, the medical oncologists' professional organization, offers patients and families a guide for making hard decisions and shows them ways to initiate helpful discussions with their oncology teams. It includes information on how to discuss with family members, including children, issues that arise in patients with advanced cancer and during end-of-life care.

Aspen Reference Group. *Pain Management: Patient Education Manual.* Aspen Publishers, 200 Orchard Ridge Drive, Gaithersburg, MD 20878; telephone: 800-638-8437; website: www.aspenpub.com.

This loose-leaf manual (in binder form) is designed to help physicians provide customized patient education on managing pain. Updates are available yearly at an additional fee.

Aspen Reference Group. *Palliative Care Patient and Family Counseling Manual.* Aspen Publishers, 200 Orchard Ridge Drive, Gaithersburg, MD 20878; telephone: 800-638-8437; website: www.aspenpub.com.

This loose-leaf manual (in binder form) is designed to help physicians provide customized patient education on palliative care topics. Updates are available yearly at an additional fee.

Scriptographic Booklets. Channing L. Bete Co., 200 State Road, South Deerfield, MA 01373-0200; telephone: 800-628-7733; fax: 800-499-6464.

Booklets are available on a wide range of topics of interest to patients with cancer and their families. Subjects include (but are not limited to) pain management, advance medical directives, social work services, hospice under Medicare, home care, long-term care, grief, depression, adult and child bereavement, and dying.

CD-Rom/DVDs

Completing a Life: An Interactive Multimedia CD-ROM for Patient and Family Education in End of Life Care. Information from www.completingalife.msu.edu.

Films Media Group, 132 West 31st Street, 17th Floor, New York, NY 10001; telephone: 800-322-8755; fax 800-678-3633; e-mail: custserv@films.com.

Before I Die: Medical Care and Personal Choices—A Fred Friendly Series

Death: An Overview

Dying with Dignity: The Sun City Choice

Letting Go: A Hospice Journey

On Our Own Terms: Moyers on Dying (4-part series)

With Eyes Open: Coping with Death (4-part series)

Looking Ahead: Choices for Medical Care When You're Seriously Ill. DVD and booklet. Developed by Health Dialog for the Foundation for Informed Decision Making. www.informedmedicaldecisions.org.

Peace of Mind: personal stories about advance directives. DVD and booklet. Developed by Health Dialog for the Foundation for Informed Decision Making. website: www.informedmedicaldecisions.org

Interested clinicians and educators can obtain a video of the entire 1997 broadcast or a special edition that is divided into segments for discussion purposes. Also available are copies of the Viewer's Guide and additional support materials to use as a study guide as part of an educational program on end-of-life issues.

Spirituality and Healing in Medicine. Harvard MED-CME, P.O. Box 825, Boston, MA 02117-0825; telephone: 617-432-1525; fax: 617-432-1562.

A series of four videotapes of a conference on Spirituality and Healing in Medicine held at Harvard Medical School in 1995. Hindu, Buddhist, Jewish, Catholic, Islamic, Hispanic-Pentecostal, Christian Science, and Seventh-Day Adventist spiritual healing practices are discussed. A much shorter overview, Healing Words, Healing Practices, *is also available.*

Websites/Databases

See also Patient and Family Bibliography.

American Medical Association. *Caregiver Self-Assessment Tool*. www.ama-assn.org.

A caregiver self-assessment tool designed to help caregivers recognize their need for home health services. Clinicians can refer caregivers to this website to help them recognize how much stress they are experiencing and to encourage them to ask for help. The tool is available in English and in Spanish.

American Society of Clinical Oncology. www.cancer.net.

This website was created by the American Society of Clinical Oncology (ASCO) for people living with cancer and for their families and friends.

Cancer Information Network. www.cancernetwork.com. Houses the journal *Oncology*.

CANCERLIT Topic Searches (National Cancer Institute). www.cancer.gov/cancerinfo.

Cansearch (National Coalition for Cancer Survivorship). www.canceradvocacy.org.

Center to Advance Palliative Care. www.capc.org.

The Center to Advance Palliative Care (CAPC) website is the resource for administrators and clinicians who wish to plan, fund, and sustain a hospital-based palliative care program. The website also lists the schedule of management-training seminars offered by CAPC.

Cochrane Collaboration. www.cochrane.org.

Reviews of research evidence, including supportive oncology and care at the end of life.

Department of Veterans' Affairs, Guide to Long-Term Care. www.va.gov/GERIATRICS/guide/longtermcare/Hospice_and_Palliative_Care.asp.

This website offers veterans information about hospice and palliative care available to them within the VHA.

Educating Physicians in End of Life Care—Oncology. www.epec.net.

The Educating Physicians in End of Life Care (EPEC) 14-module curriculum was developed and refined by the AMA. The basic EPEC program has been customized for many subspecialists, including oncologists, who can access the EPEC-Oncology modules from this site or the NCI.

End of Life Palliative Care. www.mcw.edu/palliativecare.htm.

The End of Life / Palliative Education Resource Center (EPERC)—created by the innovators at the Medical College of Wisconsin, led by Dr. David Weissman—is a comprehensive resource site for clinicians and educators. It includes peer-reviewed educational materials and the valuable Fast Facts: one-page items containing practical, useful nuggets of palliative care information and communication techniques. All the material is available at no charge.

Growth House. www.growthhouse.org/palliative.

This website has posted tools for organizations that wish to develop an outpatient palliative care program. The toolkit and blueprint from the Kaiser Permanente Program are provided, as are suggestions on how to modify the program to different organizational structures.

HealthAnswers. www.healthanswers.com.

This database, created in partnership with the American Academy of Family Physicians, contains information from the AAFP and from the American Academy of Pediatrics, the National Health Council, the National Library of Medicine, the U.S. Pharmacopoeia, the American Society on Aging, the National Alliance for Caregiving, and the National Association for Home Care. Although this database also offers materials for the lay public, many features are of interest to physicians. For example, a Health Professionals Only area, focusing on CME, contains video transcripts and graphics on several topics for which CME credit is available. MEDLINE and AIDS-LINE databases are also available, as are bulletin boards and listings of patient education materials that can be purchased.

Pain.com. www.pain.com.

Sponsored by Dannemiller Memorial Educational Foundation, this site includes interactive professional forums and chat rooms; the World Wide Congress on Pain's Virtual Library; online CME modules and accreditation; a weekly advice column; and more than 200 links to other health care sites.

PainLink. www.edc.org/PainLink.

An archival website sponsored by the Mayday Fund, a New York City foundation dedicated to relieving unnecessary pain.

Pain Medicine and Palliative Care Department at Beth Israel Medical Center. www.stoppain.org.

This website has valuable resources for pain control.

Organizations

See also Patient and Family Bibliography.

American Academy of Hospice and Palliative Medicine, 11250 Roger Bacon Drive, Suite 8, Reston, VA 20190-5202; telephone: 703-787-7718; fax: 703-435-4390; e-mail: aahpm@aahpm.org; website: www.aahpm.org.

A professional organization for physicians in many medical specialties dedicated to the advancement of hospice/palliative medicine, its practice, research, and education.

American Hospice Foundation. www.americanhospice.org.

American Pain Society, 5700 Old Orchard Road, First Floor, Skokie, IL 60077; telephone: 708-966-5595; website: www.ampainsoc.org.

Publishes Directory of Pain Management Facilities.

Hospice Foundation of America. www.hospicefoundation.org.

Hospice and Palliative Nurses Association. www.hpna.org.

Mayday Pain Resource Center, City of Hope National Medical Center, 1500 E. Duarte Road, Duarte, CA 91010; website: http://prc.coh.org.

National Hospice and Palliative Care Organization. www.nhpco.org.

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Patient and Family Bibliography

Books

General Reference

ASCOanswers. Advanced Cancer Care Planning: A Decision-Making Guide for Patients and Families Facing Serious Illness. Alexandria, Va.: ASCO, 2013.

This handbook from ASCO, the medical oncologists' professional organization, offers patients and families a guide for making hard decisions and shows them ways to initiate helpful discussions with their oncology teams. It includes information on how to discuss with family members, including children, issues that arise in patients with advanced cancer and during end-of-life care.

Babcock, Elise NeeDell. *When Life Becomes Precious: A Guide for Loved Ones and Friends of Cancer Patients*. New York: Bantam Books, 1997.

Elise Babcock founded Cancer Counseling, which has provided free professional counseling to cancer patients and their families since 1982. She has been a counselor for more than twenty years. In this highly readable book, she answers commonly asked questions about how to communicate about cancer and gives families and friends practical suggestions on what they can do to help and support not only the patient but the caregiver and other family members. It also contains a helpful listing of community resources.

Barnard, David, Anna M. Towers, Patricia Boston, and Yanna Lambrinidou. *Crossing Over: Narratives of Palliative Care*. Oxford: Oxford University Press, 2000.

Billings, J. Andrew. *Outpatient Management of Advanced Cancer: Symptom Control, Support, and Hospice-in-the-Home*. Philadelphia: J. B. Lippincott, 1985.

An outstanding resource for families who want to understand more about symptom control and psychological and social support. This book presents a unique, insightful approach to the concerns of dying patients and their families. Extensively referenced. (Out of print but copies available from some retailers.)

Buckman, Robert, in collaboration with the specialists at M. D. Anderson Cancer Center. *What You Really Need to Know about Cancer: A Comprehensive Guide for Patients and Their Families*. Baltimore: Johns Hopkins University Press, 1997.

Dr. Buckman is an experienced family physician and oncologist who has written several books on communication between people with cancer and their families, friends, and the physicians caring for them. This book is an excellent introduction to various types of cancer for people who do not have any medical background but who want to understand more about the disease and the treatments used.

Byock, Ira. *Dying Well: Peace and Possibilities at the End of Life*. New York: Riverhead Books, 1997.

Dr. Byock's inspirational book uses the narratives of patients and families he has cared for to explore the possibilities for growth even at the end of life.

Byock, Ira. *The Four Things That Matter Most: A Book about Living.* New York: Free Press, 2004.
Expanding on themes raised in Dying Well, *Dr. Byock offers a continued meditation on how families and patients can communicate the important things to each other when the patient's time is short.*

Cancer Care. *A Helping Hand: The Resource Guide for People with Cancer,* 2nd ed. Available from Cancer Care, 1180 Avenue of the Americas, New York, NY 10036-3602; telephone: 800-813-HOPE (4673) or 212-221-3300; e-mail: info@cancercare.org; website: www.cancercare.org.
A comprehensive and detailed listing of the growing number of services available across the country to people with cancer. In addition to the addresses, telephone and fax numbers, and e-mail addresses of hundreds of resources for people with cancer, each organizational listing contains a description of its mission and the services it provides.

Coleman, C. Norman. *Understanding Cancer: A Patient's Guide to Diagnosis, Prognosis, and Treatment.* Baltimore: Johns Hopkins University Press, 1998.
Dr. Coleman is professor and chairman of the Joint Center for Radiation Therapy in the Department of Radiation Oncology at Harvard Medical School. He seeks to help people with cancer prepare for encounters with physicians, understand the processes of diagnosis, and weigh the treatment options offered.

Corless, Inge B., Barbara B. Germino, and Mary A. Pittman. *A Challenge for Living: Dying, Death, and Bereavement.* 2nd ed. New York: Springer, 2005.
A compilation of essays by leaders in various disciplines on the physical, psychosocial, and spiritual needs of the patient and the caregivers, as well as the needs of the bereaved. Each essay is referenced.

Doyle, Derek. *Caring for a Dying Relative: A Guide for Families.* Oxford: Oxford University Press, 1994.
A clearly written, sensitive book from the director and consulting physician of St. Columba's Hospice in Edinburgh. It is useful for families not as a symptom management manual, but as a resource for how to deal with less tangible issues, such as visiting the cancer patient, truth-telling, the place of food and drink, "unmentionable feelings," ethical issues, and "worrying events."

Finkbeiner, Ann K. *After the Death of a Child.* Baltimore: Johns Hopkins University Press, 1996.
The author, a science writer, lost her son in a train accident when he was 18. After she had somewhat recovered, she wondered about the experiences of other parents who were similarly bereaved. She investigated thirty parents who had also lost children of different ages from various causes and shares the results of her work in this book.

Gawande, A. *Complications: A Surgeon's Notes on an Imperfect Science.* New York: Picador, 2002.
A beautifully written, insightful work. It can be recommended also for clinicians.

Halifax, Joan. *Being with Dying: Cultivating Compassion and Fearlessness in the Presence of Death.* Boston: Shambhala, 2008.
Roshi Joan Halifax, a Buddhist teacher and scholar, is known for her retreats in which she teaches clinicians and laypeople alike how to be in the presence of death. This book is a helpful introduction to her work.

Harpham, Wendy Schlessel. *When a Parent Has Cancer: A Guide to Caring for Your Children.* New York: HarperCollins, 1997.

This is actually two books, one for children (Becky and the Worry Cup) *and another that describes how to use the storybook for children of various ages. It has been highly recommended for any cancer patient who has concerns about how to discuss the cancer and the needs and fears it engenders in both the patient and the child.*

Houts, Peter S., ed. *Home Care Guide for Cancer.* Baltimore: Johns Hopkins University Press, 1996.

You can recommend this book to caregivers who need practical, step-by-step methods by which they can evaluate and manage the physical and psychosocial problems that they and the people they care for face.

Johnson, Judi, and Linda Klein. *I Can Cope: Staying Healthy with Cancer.* Minneapolis: Chronimed, 1994.

Judi and Linda developed the I Can Cope program, sponsored by the American Cancer Society. In the program, nurses and social workers guide cancer patients through the most common problems they face during and after treatment. This book will provide your patients with the core information delivered by the program, including information about cancer and its treatment and side effects, staying mentally healthy and active, communication issues, and resources available.

Levine, Margie. *Surviving Cancer.* New York: Broadway Books, 2001.

An incredibly useful narrative from a smart, strong, courageous woman who fought her cancer while maintaining her personal style and integrity every step of the way.

Lynn, Joanne, Joan Harrold, and Janice Lynch Shuster. *Handbook for Mortals: Guidance for People Facing Serious Illness.* 2nd ed. New York: Oxford University Press, 2011.

A straightforward, clearly written manual that I give to patients and families who are facing a terminal prognosis. It includes practical suggestions and seeks to empower families to get the information they need from their health care providers. It is a valuable book also for nurses and physicians who are not familiar with the demands that caring for these patients place on them and on families as they try to navigate the health care system and care for the patients at home.

Rauch, Paula, and Anna Muriel. *Raising an Emotionally Healthy Child When a Parent Is Sick.* A Harvard Medical School Book. New York: McGraw-Hill, 2006.

Remen, Rachel Naomi. *Kitchen Table Wisdom: Stories that Heal.* New York: Riverhead Books, 1996.

Remen, Rachel Naomi. *My Grandfather's Blessings: Stories of Strength, Refuge, and Belonging.* New York: Riverhead Books, 2000.

Rachel Remen is co-founder and medical director of the Commonweal Cancer Help Program. She has extensive experience in the clinical care of those who are suffering and facing life-threatening illnesses as well as in teaching undergraduate, graduate, and practicing physicians how to heal the pain of their own losses—and to become better physicians in the process. In both of these readable, engaging books, she uses stories that teach by indirection and powerfully convey her message.

Sankar, Andrea. *Dying at Home: A Family Guide for Caregiving.* Revised and expanded. Baltimore: Johns Hopkins University Press, 1999.

Dr. Sankar, a medical anthropologist, was inspired to write this book by her work as a member of a home care team for two years and by her own experience caring for a dying relative

at home. The stories she tells will be wonderfully helpful for families. They will recognize themselves in one or more of the families described, who relate how they dealt with the various problems that occurred while they cared for a dying relative at home.

Complementary Therapies

Benson, Herbert, with Marg Stark. *Timeless Healing: The Power and Biology of Belief.* New York: Scribner, 1996.

Cassileth, Barrie R. *The Complete Guide to Complementary Therapies in Cancer Care: Essential Information for Patients, Survivors and Health Professionals.* Hackensack, N.J.: World Scientific Publishing, 2011.

Dr. Cassileth is an internationally known expert on complementary medicine. This book is an extremely valuable reference tool for patients who seek these therapies, many of which can be used along with more traditional medical treatments.

Bereavement/Grief

Morris, Sue. *Overcoming Grief: A Self-Help Guide Using Cognitive Behavioral Techniques*. London: Constable & Robinson, 2008.

Sue Morris, an expert on bereavement, wrote this practical, useful guide for people who want help in dealing with their grief.

Rando, Theresa A. *Grieving: How to Go on Living When Someone You Love Dies.* Lexington, Mass.: Lexington Books, 1988.

A comprehensive, useful book designed to help those who are mourning through the process of grieving. The author includes the specific problems faced by spouses, children, friends, and significant others. Includes both resource and reference lists.

Ethics

Jonsen, A. R., M. Siegler, and W. J. Winslade. *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine.* 7th ed. New York: McGraw-Hill, 2010.

Pain

Cowles, Jane. *Pain Relief: How to Say No to Acute, Chronic and Cancer Pain!* New York: Mastermedia Limited, 1993.

Dr. Cowles is a medical journalist and patient's rights advocate who has written on a wide range of medical topics. She has had numerous experiences of inadequate pain control both for herself and her family and friends, including those suffering from cancer. After finishing this book, patients will have clear explanations for why this is so, guidelines that enable them to describe their problems to us more accurately, and lists of community and national resources on which they can call for additional help. The chapter on home care and home care resources is an unusual and especially useful one. Patients should be alert, however, to changes in addresses and phone numbers that may have occurred in the years since the book's publication.

Haylock, Pamela J., and Carol P. Curtiss. *Cancer Doesn't Have to Hurt: How to Conquer the Pain Caused by Cancer and Cancer Treatment.* Salt Lake City, Utah: Hunter House, 1997.
The authors are nurses who have worked with cancer patients for more than twenty-five years. Their book would be useful for patients and families who want an overview of what is available to optimize relief of pain, including how it can be paid for. It also contains a list of resources for managing cancer pain.

Miaskowski C, Cleary J, Burney R, et al. *Guideline for the Management of Cancer Pain in Adults and Children.* APS Clinical Practice Guidelines Series, No. 3. Glenview, Ill.: American Pain Society, 2005. www.ampainsoc.org.
This landmark publication is a consensus document prepared by the leading national pain experts from numerous clinical fields. It includes pharmacologic and nonpharmacologic techniques.

Patt, Richard B., and Susan Lang. *The Complete Guide to Relieving Cancer Pain and Suffering.* New York: Oxford University Press, 2006.
You can recommend this book to patients who need more help understanding their pain or other sources of distress or in communicating to you how they feel or wanting to use nonpharmacologic techniques. It will also reinforce what you've told them.

Religious Teachings on Pain Management and Care of the Dying

Catechism of the Catholic Church. 2nd ed. London: Continuum International, 2000.

"The Great Matter of Life and Death." *Tricycle: The Buddhist Review,* vol. 7, Fall, 1997.

Responsa of Rav Moshe Feinstein, volume 1, *Care of the Critically Ill.* Translated and annotated by Moshe Dovid Tendler. Hoboken, N.J.: KTAV Publishing, 1996.

Rinpoche, S. *The Tibetan Book of Living and Dying.* Edited by P. Gaffney and A. Harvey. New York: Harper San Francisco, 1993.

Other Books of General Interest

Albom, Mitch. *Tuesdays with Morrie: An Old Man, a Young Man, and Life's Greatest Lesson.* New York: Doubleday, 1997.
Mitch Albom writes a marvelous account of his "last course" with his former professor, who is dying of Lou Gehrig's disease (amyotrophic lateral sclerosis). The reader joins this intelligent, sophisticated, and talented author on his unsentimental journey of self-discovery and deepening appreciation for previously unexamined aspects of life.

Aries, Philippe. *The Hour of Our Death: The Classic History of Western Attitudes toward Death over the Last One Thousand Years.* New York: Knopf, 1981.

Bandeira, Manuel. *Selected Poems.* Edited and translated by David R. Slavitt. Riverdale-on-Hudson, N.Y.: Sheep Meadow Press, 2002.
Poems of love and death.

Barbery, Muriel. *The Elegance of the Hedgehog.* New York: Europa Editions, 2006.

Barnett, Terry J. *Living Wills and More.* New York: Wiley and Sons, 1992.
A guide for patients and their families who need more information on the legal requirements for ensuring that their wishes regarding medical care will be known, regardless of their medical condition.

Becker, Marilyn R. *Last Touch: Preparing for a Parent's Death.* Oakland, Calif.: New Harbinger Publications, 1992.

Ms. Becker, an MSW, offers this clearly written personal account of how she helped in her parents' final days, and how she coped with the experience.

Boethius. *The Consolations of Philosophy.* Translated by David R. Slavitt. Cambridge, Mass.: Harvard University Press, 2008.

Bone, R. C. *Reflections: A Guide to End of Life Issues for You and Your Family.* Available from National Kidney Cancer Association, telephone: 800-850-9132 or 847-332-1051; fax: 847-332-2978; website: www.nkca.org.

This free pamphlet, written by a physician who has since died of kidney cancer, is an excellent short introduction to several important issues that dying people need to address.

Broyard, Anatole. *Intoxicated by My Illness.* New York: Fawcett Columbine, 1992.

Anatole Broyard, journalist and author, died of metastatic prostate cancer. This moving, lively collection of articles deals with multiple subjects of interest to physicians, including what he expected from his own physicians, as well as a discussion of other books about cancer. It also includes a short story that mirrors Broyard's experience as one of his parents died of cancer.

Buckman, Robert. *I Don't Know What to Say . . . How to Help Support Someone Who Is Dying.* Boston: Little Brown, 1989.

Dr. Buckman is an oncologist who has particular insight into how to communicate, even about subjects that are hard to discuss. His practical suggestions will be of great benefit to friends and families of dying patients.

Cather, Willa. *Death Comes for the Archbishop.* New York: Vintage Books, 1990.

Chappell, Fred. *I Am One of You Forever.* Baton Rouge: Louisiana State University Press, 1985.

The Telegram, a chapter in this novel, describes a family's experience of loss upon learning of the death of a beloved friend.

Chappell, Fred. *Farewell, I Am Bound to Leave You.* New York: Picador, 1996.

Fred Chappell is a master poet and storyteller. In this collection of short stories, which reads like a novel, he retells the family tales told by a son-in-law to his son as they await the death of their much-beloved mother-in-law and grandmother. The first selection, The Clocks, and the end piece, The Voices, are surreal descriptions of the very real passing of a loved one.

Cousins, Norman. *Anatomy of an Illness as Perceived by the Patient: Reflections on Healing and Regeneration.* New York: W.W. Norton and Company, 1979.

de Sponde, Jean. *Sonnets of Love and Death.* Edited and translated by David R. Slavitt. Evanston, Ill.: Northwestern University Press, 2001.

Dubler, Nancy, and David Nimmons. *Ethics on Call.* New York: Harmony Books, 1992.

A medical ethicist shows how to take charge of life-and-death choices.

Ephron Nora. *I Remember Nothing and Other Reflections.* New York: Knopf, 2010.

Hall, Donald. *Without.* New York: Houghton Mifflin, 1998.

Kabat-Zinn, J. *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness.* New York: Dell, 1990.

A complete, step-by-step guide describing the philosophy and the day-to-day program of the Stress Reduction Clinic founded by Dr. Kabat-Zinn at the University of Massachusetts Medical Center.

Ko, A., E. Rosenbaum, M. Dollinger. *Everyone's Guide to Cancer Therapy: How Cancer Is Diagnosed, Treated, and Managed Day-to-Day.* 5th ed. Kansas City, Miss.: Andrews McMeel, 2008.

Kübler-Ross, E. *On Death and Dying.* New York: Collier Books, Macmillan, 1969.

LeShan, Lawrence. *Cancer as a Turning Point: A Handbook for People with Cancer, Their Families, and Health Professionals.* Rev. ed. New York: Plume/Penguin, 1994.

Dr. LeShan is a psychotherapist with more than thirty-five years of experience in working with cancer patients. His book may be useful for those of your patients who are interested in exploring their inner life; it includes a workbook full of exercises to help them do this.

Lynch, Thomas. *The Undertaking: Life Studies from the Dismal Trade.* New York: Penguin Books, 1997.

Mercier, Pascal. *Night Train to Lisbon*. New York: Grove Press, 2004.

"A handbook for the soul, intellect, and heart."

Nuland, Sherwin B. *How We Die: Reflections on Life's Final Chapter.* New York: Knopf, 1994.

You'll find Dr. Nuland's book especially valuable for those patients or families who have never seen anyone die and want to know what it will look like. The book contains much more than this and will be of interest to those who can deal with its graphic details.

Oliver, Mary. *New and Selected Poems: Volume One.* Boston: Beacon Press, 1992.

Pastan, Linda. *Carnival Evening: New and Selected Poems, 1968–1998.* New York: W. W. Norton, 1998.

The poem "The Five Stages of Grief" is of special interest to those of us trying to understand how to help our bereaved patients.

Peck, M. Scott. *Denial of the Soul: Spiritual and Medical Perspectives on Euthanasia and Mortality.* New York: Harmony Books, 1997.

M. Scott Peck, author of, among many other works, The Road Less Traveled, *deals with the difficult subjects of emotional pain, euthanasia, and the importance of the soul. His is a thoughtful discussion that would be of interest to those engaged in the debate about physician-assisted suicide.*

Price, Reynolds. *A Whole New Life: An Illness and a Healing.* New York: Atheneum, 1994.

A cautionary tale for physicians by novelist and short story writer Reynolds Price, who had locally advanced cancer; he chastises us for what he terms our "clinical distance."

Quill, Timothy. *A Midwife through the Dying Process: Stories of Healing and Hard Choices at the End of Life.* Baltimore: Johns Hopkins University Press, 1996.

Dr. Quill shares with the reader many moving stories of the people he has cared for.

Roth, Philip. *Patrimony.* New York: Simon & Schuster, 1991.

A wonderful revelation of Philip Roth's relationship with his father—their time together when Roth was a child and the years in which his father's life was profoundly altered by a rare brain tumor. Roth was the primary caregiver for his father during this time, and he writes about the experience as only he can.

Sophocles. *The Theban Plays of Sophocles*. Translated by David R. Slavitt. New Haven, Conn.: Yale University Press, 2007.

All three are wonderful, but read Oedipus at Colonus *with particular attention.*

Stahl, Bob, and Elisha Goldstein. *A Mindfulness-Based Stress Reduction Workbook*. Oakland, Calif.: New Harbinger, 2010.

An easy-to-use workbook with extremely compelling meditations on impermanence, anxiety and stress, and other issues. Includes an MP3 CD with 21 guided meditations. *Terrific aid to a self-care practice.*

Stone, John. *Where Water Begins: New Poems and Prose.* Baton Rouge: Louisiana State University Press, 1998.

Sulmasy, D. P. *The Healer's Calling: A Spirituality for Physicians and Other Health Care Professionals.* New York: Paulist Press, 1997.

Daniel Sulmasy is a philosopher, a health services researcher, a Franciscan friar, and a medical oncologist. In this eloquent, thoughtful book he relates his "personal experience of being a man of faith engaged in the work of a health care professional" as a basis for our own self-explorations. Chapters include Spirituality and the Health Care Professional; Medicine, Love and the Art of Being Uncertain; The Wine of Fervent Zeal and the Oil of Compassion; God-Talk at the Bedside; Prayer and the Five Senses: A Physician's Meditation; Suffering, Spirituality, and Health Care; and Wounded Healers.

Verghese, A. *My Own Country.* New York: Simon & Schuster, 1994.

The odyssey of a young physician who chooses to care for patients with AIDS in the rural South, its effect on him and his family, and on his patients and their families.

Webb, Marilyn. *The Good Death: The New American Search to Reshape the End of Life.* New York: Bantam, 1997.

Marilyn Webb is an investigative journalist who spent six years exploring this topic. In this almost 500-page volume, she shares the stories of patients and families for whom death provided the opportunity for either growth or unremitting pain and explains the many factors that contributed to such different outcomes. She outlines the components of a good experience, barriers to be overcome, and allies to seek along the way.

CD-Roms/ DVDs

Completing a Life: An Interactive Multimedia CD-ROM for Patient and Family Education in End of Life Care. Information from www.completingalife.msu.edu

Films Media Group, 132 West 31st Street, 17th Floor, New York, NY 10001; telephone: 800-322-8755; fax 800-678-3633; e-mail: custserv@films.com.

Before I Die: Medical Care and Personal Choices—A Fred Friendly Series

Death: An Overview

Dying with Dignity: The Sun City Choice.

Letting Go: A Hospice Journey

On Our Own Terms: Moyers on Dying (4-part series)

With Eyes Open: Coping with Death (4-part series)

Looking Ahead: Choices for Medical Care When You're Seriously Ill. DVD and booklet. Developed by Health Dialog for the Foundation for Informed Decision Making. www.infor medmedicaldecisions.org.

Peace of Mind: Personal Stories about Advance Directives. DVD and booklet. Developed by Health Dialog for the Foundation for Informed Decision Making. www.informedmed icaldecisions.org

Websites and Databases

ABCD—Americans for Better Care of the Dying. www.abcd-caring.org.

American Cancer Society. www.cancer.org.

American Medical Association. *Caregiver Self-Assessment Tool*. www.ama-assn.org.

A caregiver self-assessment tool designed to help caregivers recognize their need for home health services. Clinicians can refer caregivers to this website to help them recognize how much stress they are experiencing and to encourage them to ask for help. The tool is available in English and in Spanish.

American Society of Clinical Oncology: Cancer.net.

ASCO's website for people living with cancer and for their families and friends.

Candlelighters Childhood Cancer Foundation. www.candle.org.

Information on written materials, more than 400 peer support groups, and contacts for all family members nationwide.

Caregiver Action Network. www.caregiveraction.org.

Caregiver Survival Resources. www.caregiver.com.

Caring Connections. www.caringinfo.org.

This website is the National Hospice and Palliative Care Organization's (NHPCO) website for caregivers and patients.

Catholic Health Association of the United States. www.chausa.org.

Center to Advance Palliative Care. www.capc.org.

This website has posted tools for organizations that wish to develop palliative care programs in the inpatient or outpatient setting.

Counseling for Loss and Life Changes. www.counselingforloss.com.

Crisis, Grief & Healing. www.webhealing.com.

A web page created by psychotherapist Tom Golden.

Department of Veterans' Affairs, Guide to Long-Term Care. www.va.gov/GERIATRICS/guide/longtermcare/Hospice_and_Palliative_Care.asp.

This website offers veterans information about hospice and Palliative Care available to them within the VHA.

Dying Well. www.dyingwell.com.

ElderWeb. www.elderweb.com.

Growth House. www.growthhouse.org/palliative.

The best website for information on palliative and end-of-life care, with extensive links to other websites. Includes professional forums, electronic versions of books, an electronic bookstore, and information on hospice, palliative care, pain, and grief. Telephone number for healthcare providers: 415-863-3045.

HealthAnswers. www.healthanswers.com.

This database was created in partnership with the American Academy of Family Physicians. It contains an online U.S. Pharmacopoeia drug reference and links to caregiving and patient support sites. The HealthAnswers Knowledge Base can be searched, like a CD-ROM, for information on an extensive variety of conditions.

Last Acts—Care and Caring at the End of Life. www2.edc.org/lastacts.

Medicare Rights Center. www.medicarerights.org.
Provides free counseling services for Medicare beneficiaries who cannot afford private assistance.
National Coalition for Cancer Survivorship. www.canceradvocacy.org.
OncoLink. www.oncolink.upenn.edu.
Pain Medicine and Palliative Care at Beth Israel Medical Center, www.stoppain.org.
This website provides valuable clinical and educational resources for pain control, palliative care, and hospice. Telephone: 212-844-8970.

Organizations

After Breast Cancer Diagnosis (ABCD), 5775 N Glen Park Road, Suite 201, Glendale, WI 53209; telephone: 414-977-1780; helpline: 800-977-4121; website: www.abcdbreastcancersupport.org.
American Academy of Hospice and Palliative Medicine, 4700 W. Lake Ave., Glenview, IL 60025; telephone: 847-375-4712; website: www.aahpm.org.
American Brain Tumor Association, 2720 River Road, Suite 146, Des Plaines, IL 60018; telephone: 800-886-2282; website: www.abta.org.
American Cancer Society, 1599 Clifton Road NE, Atlanta, GA 30329 (national office); telephone: 800-227-2345 (call for phone number of local division); website: www.cancer.org.
American Childhood Cancer Organization, National Office, P.O. Box 498, Kensington, MD 20895-0498; website: www.acco.org.
American Foundation for Urologic Disease, 300 West Pratt Street, Suite 401, Baltimore, MD 21201-2463.
For information on cancer of the prostate and bladder.
American Hospice Foundation, 2120 L Street NW, Suite 200, Washington, DC 20037; website: www.americanhospice.org.
American Society of Clinical Hypnosis, 140 N. Bloomingdale Road, Bloomingdale, IL 60108-1017; telephone: 630-980-4740; website: www.asch.net.
Bloch Cancer Foundation, 4410 Main Street, Kansas City, MO 64111; telephone: 816-932-8453; website: www.blochcancer.org.
Cancer Care, 1180 Avenue of the Americas, New York, NY 10036; telephone: 212-221-3300; website: www.cancercare.org.
See also Cancer Care Counseling Line, listed under Support Groups.
Cancer Information Service, National Cancer Institute, Office of Cancer Communications, Center Drive, Building 31, Room 10A10, Bethesda, MD 20892-2580; website: www.cancer.gov/aboutnci/cis.
Caregiver Action Network, 2000 M St. NW, Suite 400, Washington, DC 20036; telephone: 202-772-5050; website: caregiveraction.org.
City of Hope Medical Center, 1500 East Duarte Road, Duarte, CA 91010-0269; telephone: 626-256-4673; website: www.cityofhope.org.
Compassionate Friends; telephone: 410-560-3358; website: www.compassionatefriends.org.
A self-help group for survivors of suicides.
Hospice Association of America, 228 7th Street SE, Washington, DC 20003; telephone: 202-546-5419; website: www.hospice-america.org.

Hospice Foundation of America, 2001 S Street NW, #300, Washington, DC 20009; telephone: 800-854-3402; website: www.hospicefoundation.org.

Hospice and Palliative Nurses Association, Penn Center West One, Suite 229, Pittsburgh, PA 15276; telephone: 412-787-9301; website: www.hpna.org.

International Myeloma Foundation, 12650 Riverside Drive, Suite 206, North Hollywood, CA 91607-3421; telephone: 800-452-2873; website: www.myeloma.org.

Leukemia and Lymphoma Society, telephone: 800-955-4572; website: www.lls.org.

Lymphoma Research Foundation of America, Inc., 8800 Venice Boulevard, Suite 207, Los Angeles, CA 90034; telephone: 310-204-7040.

National Brain Tumor Foundation, 22 Battery Street, Suite 612, San Francisco, CA 94111-5520; telephone: 415-834-9970; website: www.braintumor.org.

National Breast Cancer Coalition, 1101 17th Street NW, Suite 1300, Washington, DC 20036; telephone: 202-296-7477; website: www.natlbcc.org.

National Cancer Institute Cancer Information Service; telephone: 800-422-6227; fax: 301-402-5874 (CANCERFAX); website: www.cancer.gov.

National Cancer Institute Publications Ordering Service, P.O. Box 24128, Baltimore, MD 21227; telephone: 800-4CANCER (800-422-6237).

Easy-to-read booklets are available free of charge. Get Relief from Cancer Pain *and* Helping Yourself during Chemotherapy *are available in large print for those who are visually impaired.*

National Hospice and Palliative Care Organization. www.nhpco.org.

National Kidney Cancer Association, 1234 Sherman Avenue, Suite 203, Evanston, IL 60202; telephone: 800-850-9132; website: www.nkca.org.

National Ovarian Cancer Coalition, 500 NE Spanish River Boulevard, Suite 8, Boca Raton, FL 33431; telephone: 888-OVARIAN (888-682-7426); fax: 561-393-7275; e-mail: NOCC@ovarian.org; website: www.ovarian.org.

Support Groups

American Cancer Society, National Office, 1599 Clifton Road N.E., Atlanta, GA 30329; telephone: 800-227-2345; website: www.cancer.org.

Send for Guidelines on Support and Self-Help Groups, *1995.*

Cancer Care, 1180 Avenue of the Americas, New York, NY 10036; telephone: 800-813-HOPE (4673) or 212-221-3300; website: www.cancercare.org.

An organization that offers free counseling and other services to cancer patients and their families. Staffed by social workers.

Cancer Care Counseling Line; telephone: 800-813-4673 (800-813-HOPE); Mon. to Fri., 9 a.m. to 5 p.m. EST; e-mail: CancerCare@aol.com.; www.cancercare.org

This is a free counseling line sponsored by Cancer Care, through which callers can receive one-to-one counseling from experienced oncology social workers, as well as referrals, free educational materials, and information on telephone support groups and educational seminars. All Cancer Care services are free of charge.

Cancer Information Service; telephone: 800-4CANCER (800-422-6237); TTY: 800-332-8615.

This is the National Cancer Institute's national telephone service; staff answer questions in English and Spanish and distribute NCI materials.

Mautner Project of Whitman-Walker Health, 1707 L Street NW, Suite 1060, Washington, DC 20036; telephone: 202-332-5536 (voice/TTY); fax: 202-265-6854; website: www.whitman-walker.org/mautnerproject.

From the website: "The Mautner Project of Whitman-Walker Health is committed to improving the health of women who partner with women including lesbian, bisexual and transgender individuals, through primary medical care, support services, education and advocacy."

National Women's Health Network, 514 10th Street NW, Suite 400, Washington, DC 20004; telephone: 202-347-1140; website: www.womenshealthnetwork.org.

Office of Minority Health Resource Center, U.S. Department of Health and Human Services, P.O. Box 37337, Washington, DC 20013-7337; telephone: 800-444-6472; website: http://minorityhealth.hhs.gov.

Provides information on health resources at federal, state, and local levels.

US TOO! International, 930 North York Road, Suite 50, Hinsdale, IL 60521; telephone: 800-80-USTOO (800-808-7866); www.ustoo.com.

Provides prostate cancer education and support.

Cancer Support Community, 919 18th Street NW, Suite 54, Washington, DC 20006; telephone: 202-659-9709 or 888-793-9355; website: www.cancersupportcommunity.org.

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